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OF THE

AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 78th ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN BALTIMORE, DURING WEEK OF MAY 5, 1930.

The 1930 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conferences of Pharmaceutical Association Secretaries and of Pharmaceutical Law Enforcement Officials will also be held at Baltimore, same time and place.

For Association Roster and Roster of the Boards of Pharmacy, of Officers of Pharmaceutical Associations, Local Branches, see pages x, xii, xiv, etc.

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THE SERVICE OF PHARMACY.

THE PHARMACOPŒIAL CONVENTION OF 1930.

THE 1930 Convention should be an event in the life of every physician and pharmacist of this great country; for it brings into being the mighty movement of unparalleled importance to American medicine and to American pharmacy. The word "should" employed above is used advisedly. Even though the substitution of the words "is not" for "should be" expresses a close approximation of the truth, the fact still remains that the two or three hundred thousand persons interested in medicine and in pharmacy and the millions of patients and customers are enormously affected by the *raison d'etre* of the Pharmacopœial Convention; the book that eventually emanates from the Committee of Revision: the United States Pharmaceopœia. It is therefore earnestly hoped that both physicians and pharmacists take sufficient interest in the 1930 Convention to see that full delegations are appointed from each of the several authorized bodies; medical colleges and state medical associations, pharmacy colleges and state pharmaceutical associations; national associations, medical, pharmaceutical, dental and chemical; the various scientific bureaus of the national government; and that these delegations consist of representative men and women pledged to devote the time and money necessary for the trip to Washington and to the week of deliberations that will start the machinery producing U. S. P. XI.—H. V. Arny, in October *American Druggist.*

PROFESSIONAL PHARMACY.

(From *International Health Year Book, 1928.*)

"AS IN THE case of medicine and dentistry, the standards of pharmacy have also greatly advanced in the United States. Colleges of pharmacy were first organized in this country between 1820 and 1830. At that time and for many years later pharmacy was generally learned by the apprenticeship method. Prior to 1875, when the various states began to enact laws regulating the practice of pharmacy, anyone could establish and conduct a drug store. The number of colleges of pharmacy has gradually increased to more than 60, and the standards have advanced until graduation from high school and completion of not less than a three-year approved course in pharmacy are required by most states as prerequisite to examination for license.

"The AMERICAN PHARMACEUTICAL ASSOCIATION, an organization based upon high professional ideals, has aided in raising the standards of the profession. This ASSOCIATION now seventy-six years old, has also contributed to the improvement of the Pharmacopœia of the United States, the official standard for drugs and medicines, and it compiles and issues the National Formulary, which standardizes the non-official drugs and preparations in use by physicians, with respect to Latin titles and to formulæ."

VAUQUELIN CENTENARY.

LOUIS NICOLAS VAUQUELIN became director of the School of Pharmacy of Paris in 1803. We have a reference stating that in 1822 he left Paris and did not return until 1827; he died in 1829. "Wooten's Chronicals" record that Vauquelin was director of the School of Pharmacy until his death, in 1829. It seems that there is an error in one or the other statement, which should be corrected. He is best known to pharmacists for his investigations of belladonna, cinchona, ipecac and other alkaloidal drugs. Caventou was one of his many students, well known to pharmacy and chemistry. Vauquelin began work as porter in a Rouen pharmacy.

R. L. SWAIN.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

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THE CHAIRMAN OF THE HOUSE OF DELEGATES.

Robert Lee Swain, son of the late Rev. C. P. Swain and Martha H. Swain née Messick, was born at Redden, Sussex County, Del., September 29, 1887. After graduation from the Dover High School he entered the School of Pharmacy of the University of Maryland from which he graduated in 1909. Sometime after his graduation, Dr. Swain purchased a pharmacy in Sykesville, Md., which he conducted until 1927, when his other duties made it necessary to give up this activity.

Early in his professional career, organization activities gained Dr. Swain's interest and support and he has been a member of the Maryland Pharmaceutical Association and the AMERICAN PHARMACEUTICAL ASSOCIATION for many years. In the former, he held many committee appointments and, in 1925, was elected Editor of its official publication, the *Maryland Pharmacist*, which he has made an outstanding state journal. He has been a regular attendant at the meetings of the A. PH. A., served for two years as President of its Baltimore Branch, was elected Vice-Chairman of the House of Delegates in 1928, and Chairman in 1929.

In 1920, upon recommendation of the state association, Governor Ritchie appointed Dr. Swain a member of the Maryland Board of Pharmacy and reappointed him in 1925, since which time he has served as its Secretary-Treasurer. He has taken an active interest in the National Association Boards of Pharmacy and is now in charge of its latest added activity, the post-graduate instruction to be furnished by the Association to the board members.

When the enforcement of the Maryland laws affecting pharmacy was placed under the State Department of Health, following the membership of a pharmacist on the Board of Health, in 1922, Dr. Swain was elected Deputy Food and Drug Commissioner in charge of this enforcement, and has discharged this important office since that time. The experience gained in this work brought about his suggestion of the need for closer contacts between the pharmaceutical enforcement officials of the several states which led to the establishment at the 1929 meeting of the A. PH. A. of the Conference of Pharmaceutical Law Enforcement Officials, of which he was elected the first Chairman.—E. F. K.

EDITORIAL

E. G. EBERLE, EDITOR 10 West Chase St., BALTIMORE, MD.

THE UNITED STATES PHARMACOPŒIA XI AND NATIONAL FORMULARY VI.

IT IS unnecessary to stress the fact that the AMERICAN PHARMACEUTICAL ASSOCIATION is deeply interested in the revisions of the standards for drugs and preparations, represented by the United States Pharmacopœia and National Formulary.

It may be stated that a motive for organizing the AMERICAN PHARMACEUTICAL ASSOCIATION was the desire of pharmacists to improve the quality of drugs and medicines and that this has continued to be one of its principal activities.

The ASSOCIATION accepts full responsibility for the revision of the National Formulary, hence it is a matter of very deep concern to every member. A committee to have charge of the Sixth Edition was elected at the recent annual meeting and is now organizing for this very responsible duty. Fullest coöperation should be given the Committee by all pharmacists so that the National Formulary may continue to serve efficiently as a legal standard, and that its purpose may be fully understood by physicians and pharmacists. In the spirit of service it is said that its usefulness should not be limited to the official recognition of the Materia Medica, which is a very important and a distinctive recognition, but there should be more extended prescribing of its preparations by physicians in their practice. The outstanding aim is to have the National Formulary serve its purpose as a representative work of professional pharmacists, and thereby the AMERICAN PHARMACEUTICAL ASSOCIATION renders an essential service to the Government, states and the public.

The revision of the United States Pharmacopœia is entered into by the AMERICAN PHARMACEUTICAL ASSOCIATION as a service in which the divisions of Medicine, Pharmacy and the Drug Industry share; important to all of them, as well as the Federal Government and states for the protection of their citizens and safeguarding their health, and promoting medical and pharmaceutical practice. In fixing the standards for drugs and chemicals the Committee contributes largely to the commerce and industries. There is no question relative to the sincerity of all who are delegates to the Pharmacopœial Convention; however, no objection will be made to the suggestion that they carefully study revision problems; it is assumed that they will give due consideration to the disinterested selection of members for the Committee of Revision and the Board of Trustees. A representative and large delegation testifies to a general interest, and as a result the Pharmacopœia XI will reflect the status of medicine and of pharmacy and serve the public accordingly. The former revisions of the Pharmacopœia represent a heritage of which we avail ourselves and, after the completion of our work, pass on to the next generation.

The Pharmacopœia and National Formulary have recognition as legal standards in the Federal and State laws applying to drugs and preparations of them, and the designation "official" is applicable, equally, to both standards. Such

recognition makes it imperative that the interest of the public be given due consideration in the revision of both standards and that they should be looked upon by physicians and pharmacists as public trusts.

BIOLOGICAL STANDARDIZATION.

THE AMERICAN PHARMACEUTICAL ASSOCIATION does not assume a partisan attitude upon controversial questions, but it can investigate such subjects in the search for truth, and when this is made plain controversy ceases. The foregoing statement, made in substance by another, may be applied to some of the biological tests relative to which there are differences of opinion. A purpose of the publication of a series of articles relating to biological standardization is search for truth. In the October number of the JOURNAL, Aconite was the subject of two papers; in this issue Ergot and, if possible, Digitalis will receive consideration. The constant interest of the ASSOCIATION in U. S. P. Revision work is evidenced by its coöperation in publishing researches in the JOURNAL and "Abstracts of Changes" in the Pharmacopœia, during the revision periods, whereby the information is communicated to those interested. The same applies to the National Formulary, wherein the AMERICAN PHARMACEUTICAL ASSOCIATION has the responsibility of revision and publication.

Evidently a number of questions are involved in the proper standardization of ergot and its preparations. Much experimental work has been reported on this important drug for more than a half century; the clinical results have varied and experiences in the laboratories have not always been consistent. These reports have stimulated a closer study of the drug and its preparations, and recent investigations seem to explain some disagreements of former investigators. The importance of the drug, it is hoped, warrants the number of pages given to the researches reported to the Scientific Section at the Rapid City meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION. Pharmacists have responsibilities in proper standardization of drugs and, hence, this is a subject of paramount interest; it is an expression of professionalism in pharmacy.

"IRREGULAR LEGISLATIVE SCHEMES."

The *Army and Navy Register* criticizes the Pharmacy Corps Bill as follows:

"One of the circumstances that beset Congress, to the annoyance of those of the legislative and appropriations' committees and to the impairment of really necessary and worthy projects that inevitably crowd the calendars of the House and Senate, is that which finds every session confronted with measures that have little or no merit, that come from various unknown and even unknowable sources and that have no indorsement from the executive officials, who have a responsibility for recommending legislation required for the protection, development, and conduct of the Government. A few of these types of measures pass both branches of Congress, and there may be instances where they receive presidential approval.

"One of the most conspicuous of these examples of unauthorized, undesired and unnecessary measures was that which failed of enactment in the 70th Congress, the bill, of more or less mysterious authorship, intended to impose on the War Department a new bureau for the administra-

tion of the affairs of the Organized Reserves. It never acquired the favorable comment of the then Secretary of War, Mr. Davis, whose silence in this particular was among the most unaccountable of departmental inarticulation.

"Of much less importance and of correspondingly little consequence was another measure (H. R. 16278), introduced by Mr. Kelly, of Pennsylvania, to provide officers and enlisted men for a pharmacist corps in the Army. It is of no special interest at this time, and evidently made no impression upon the House military committee in its hearings on this bill, that accusations were made that Army medical officers issued prescriptions for drugs that were defective and a peril to the life of the patient. The bill originated in a quarter not revealed, and accordingly it was left to surmise that it was sanctioned and urged by the Association of Pharmacists. While there was nothing in this instance of needless legislation to criticise for its ulterior and harmful purpose, it belongs to that class of measures that should never be introduced and submitted for committee discussion until those interested in it ascertain from the responsible officials whether or not it possessed the qualities asserted in its behalf by its sponsors and whether or not it would prove an interference with other legislation already under consideration. By the simplest process imaginable the unfavorable attitude of the Secretary of War would have been promptly and convincingly disclosed. The bill was plausible enough in its provisions and in the accompanying arguments and charges, but almost casual inquiry made in the proper place would have shown the futility and possible menace of such an endeavor, the purposes of which were more efficiently met to the greater advantage of the civilian pharmacists, for example, in the measure of general effect drafted by the surgeon general of the Army and introduced in the last days of the 70th Congress by Representative Wainwright and again in the present Congress (H. R. 1248) on April 18."—*Army and Navy Register*, November 1929.

FOR years the conditions existing in the United States Army in the matter of pharmaceutical practice, embracing the compounding of physicians' prescriptions, the dispensing of drugs, poisons and potent medicinal agents and the general handling of supplies for the sick, have been notoriously unsatisfactory to pharmacists. Notwithstanding the efforts of the AMERICAN PHARMACEUTICAL ASSOCIATION and other organizations including the American Medical Association to bring about the necessary improvement, the military authorities make poor pretense of providing a pharmaceutical service worthy of the name. In civil life a rigid standard of competency is demanded of those engaged in this responsible and essential work; in the Army in most instances work of this character is left in the hands of persons having inadequate training, insufficient experience and correspondingly lacking in the rudimentary phases of professional fitness. The military authorities have treated the entire subject with a marked and callous indifference, and the efforts of those who have attempted to call attention to the dangers of the present system have been shunted aside as worthy of no consideration.

The bill for the proposed pharmacy corps is classed with "Irregular Legislative Schemes" in the editorial of the *Army and Navy Register*, quoted above. The undertaking is referred to as having "little or no merit" and as having sprung from "unknown and even unknowable sources." The bill is further characterized as "having no endorsement from the executive officials, who have a responsibility for recommending legislation required for the protection, development and conduct of the Government." In spite of its basic humanitarian aspects, the *Army and Navy Register* casts the bill aside as of "no importance and correspondingly little consequence," and continues with the statement that the bill "is of no special interest at this time, etc.," as above quoted, in full.

If written with a full knowledge of the facts, the editorial exhibits an amazing inability to understand and interpret them; if written by one unfamilar with the

subject, the article is glaringly unfair and unworthy of a discussion of a serious purpose. The source of the bill has not been hidden; quite the opposite, in fact. The AMERICAN PHARMACEUTICAL ASSOCIATION, at its 1928 convention, held at Portland, Maine, gave earnest study to the conditions underlying this bill, and gave its enthusiastic endorsement to the measure, presented by a committee of experts which the ASSOCIATION had appointed to deal with this matter. The measure has been approved by practically every national and state pharmaceutical organization. The AMERICAN PHARMACEUTICAL ASSOCIATION has behind it three-quarters of a century of splendid accomplishment. Thus the charge that the bill sprung from "unknown and even unknowable sources" impugns the information on which the *Army and Navy Register* bases its opinion. In a letter, dated October 17, 1928, addressed to Mr. A. L. I. Winne, chairman of the committee appointed to bring about a Pharmacy Corps in the Medical Department of the United States Army, Surgeon General Ireland stated that "under the circumstances I am now and will be as long as I am Surgeon General opposed to the organization of a corps of pharmacists in the Medical Department of the United States Army." An effort was made to stimulate the interest of the military authorities in the purposes of the bill, so another insinuation of the *Army and Navy Register* falls as not in keeping with the facts.

As the matter now stands, the Army of the United States is a place where in our opinion proper and adequate safeguards are not thrown about the exacting and responsible duties of those engaged in pharmaceutical work. In civil life the laws of every state regard this work as seriously related to the welfare of the people. Colleges of Pharmacy are important units in many of the outstanding educational institutions of the country. More than two thirds of the states require a standard university degree in pharmacy as one of the requisites of exacting and stringent standards for pharmaceutical practice and all of them require that the pharmacist prove his fitness and reliability by an examination before being registered. In addition, the laws of most of the states provide for the active enforcement of the pharmacy laws so that the protection contemplated by the statutes may be in fact provided.

The relation existing between the *Army and Navy Register* and the military departments of our Government is unknown to us and we cannot judge how correctly it reflects views of the responsible heads of these departments. The Surgeon General of the Army occupies a unique position and the *Army and Navy Register* voices sentiments that are difficult to understand by those who know the dangers and responsibilities involved in handling drugs and medicines. If the responsible authorities approve these expressions the conclusion is unescapable that continued adherence to military principles and the persistent endorsement and defense of antiquated military procedure induce a certain indifference to human welfare. It is obvious that life, health and happiness are not given the same high value in military circles that is accorded these priceless possessions in civil life where a human being is still a human being irrespective of his position in the social cosmos.—R. L. SWAIN, *Chairman*, A. PH. A. Committee on Pharmacy Corps in the Medical Department, U. S. Army.

SCIENTIFIC SECTION

THE PHARMACOLOGY OF ERGOT: WITH PARTICULAR RESPECT TO ITS BIOLOGICAL ASSAY AND STANDARDIZATION.*

(The bibliography will follow the last article of the series.)

I. THE PRESENT STATUS OF ERGOT.

BY MARVIN R. THOMPSON.[1]

INTRODUCTION.

During the past fifty years a vast amount of experimental work has been reported upon the pharmacological and clinical properties of ergot of rye. As a drug it is comparatively well known, having been used in medicine for a great many years, principally as a parturient or parturifacient in the treatment of post-partum hemorrhage, because of its specificity in producing contraction of the uterus, especially in the gravid state.

In spite of the fact that the drug has been found to be highly specific in its physiological and clinical reactions, in recent years it has fallen into more or less disrepute as a medicinal agent, largely because of certain inconsistencies and irregularities arising from its use. Posterior pituitary substance has been found to possess similar clinical properties with a less uncertainty in connection with its therapy, and has, therefore, threatened to replace ergot, especially in obstetrics.

From the amount of ergot imported and used in this country alone in recent years, however, it is clearly evident that this drug still occupies an important place in medicine as a parturient and also as an emmenagogue. Since no substitutes have supplanted its use in therapeutics, it is obvious that the valuable and important properties of the drug still receive recognition.

Because of this evident value of ergot in medicine, and the highly specific nature of the drug as shown in clinical and pharmacological studies, the unsuccessful use of the drug in most instances is believed to be due to lack of knowledge concerning the preparations used, and the inconsistencies in reactions exhibited by its galenicals may be logically ascribed to one or more of the following factors: 1st, that individual samples of the crude drug are inconsistent in regard to the amount or proportion of active principles contained therein; 2nd, that the processes involved in the preparation of its galenicals are faulty in that they do not always uniformly extract the specific active principle or principles; 3rd, that the methods used for the standardization or adjustment of potency do not accurately measure the clinically active constituents; 4th, that one or more of the active principles may seriously interfere with the clinical effect of the others, or interfere in the measurement of potency by the currently used bio-assay methods; 5th, that the medicinally valuable principles are of such an unstable nature that they do not appear in the preparations in defined amount by the time they are administered to the patient due to deterioration of the active agents.

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* Scientific Section, A. PH. A., Rapid City meeting, 1929.

[1] Assistant Pharmacologist, Pharmacological Laboratory of the Food, Drug and Insecticide Administration; U. S. Department of Agriculture, Washington, D. C.

In an attempt to determine which of these factors are responsible for the clinical and pharmacological inconsistencies or irregularities, the author has conducted an intensive investigation of the pharmacological properties of ergot of rye during the past two years. The results of these experiments, it is believed, explain many of the currently existing disagreements among clinicians and pharmacologists regarding the nature of its reactions.

In reviewing the earlier literature upon ergot, one encounters such a long series of conflicting results and differences of opinion that the subject is truly bewildering, particularly that dealing with the active principles found in the drug, and the chemical nature and pharmaco-dynamic activity ascribed thereto.

During the past 25 years, several investigators have greatly overcome the previously existing chaos by a re-interpretation of the earlier results of others, which was made possible only by intensive research. Barger and Dale (6), in 1907, published a remarkably enlightening interpretation of earlier literature upon the constituents of ergot together with their own observations, which, together with more recent work, quite definitely established that the specific active constituents of ergot were alkaloidal in nature. Very recently Barger (35) published the History of Ergot, an excellent review of the status at present. Since the isolation of these alkaloids in Europe by Tanret, Barger and Stoll, a great deal of information regarding the chemical and physiological nature of these alkaloids has been made available by these as well as other investigators. The different names which have been applied to these alkaloids, and also the conflicting reports concerning the pharmaco-dynamic activity of these various constituents and ergot galenicals have rendered the literature very confusing owing perhaps to results obtained from impure mixtures of the constituents and the great variations exhibited in the response of the various animals and methods used in pharmacological studies.

THE PHYSIOLOGICALLY ACTIVE CONSTITUENTS OF ERGOT.

The constituents of ergot which are responsible for the pharmaco-dynamic activity of its preparations may be conveniently divided into two groups, 1st, a series of alkaloids, and 2nd, a series of amines or amino bases. The crude drug contains appreciable quantities of a fixed oil, varying from 10 to 30 per cent, in addition to a coloring principle commonly known as sclererythrin.

The identity of these active constituents, with the chemical and pharmacological natures thereof, have been the subjects of intensive research for over a hundred years, and much remains to be done before even the more recent evidence set forth will be universally accepted as knowledge among the scientific investigators interested in ergot. However—although many phases remain disputed or unknown—all of the work has not been in vain.

At the present time it seems generally agreed that the alkaloids are the specific constituents responsible for the clinical activity of the drug (1). At least four different alkaloids have been identified with the drug, but the activity is believed to be due to but two, ergotoxine (3) and ergotamine (5). The other two, ergotinine (2) and ergotaminine (5) have been found to be relatively inactive by Kobert (7) and Spiro (5), respectively. The hydro-ergotinine of Kraft (4) has been shown to be identical with ergotoxine (6). Ergotoxine and ergotamine are active both orally and hypodermically.

It is further agreed that the proteinogenous amines identified with ergot are not responsible for the desirable clinical effects of ergot preparations. Indeed, they are regarded as being non-specific for the drug since they do not always occur in freshly collected material. Spiro and Stoll (5) and Stoll and Rothlin (9) have found their presence inconstant. The most important of these non-specfic amines are histamine, tyramine, acetyl-, and possibly other cholines, histamine being of the greater importance because of its greater activity and occurrence (1). Their activity by oral administration is doubtful (14).

The literature concerning the pharmaco-dynamic activity and chemical natures of all of these constituents has been reviewed by several investigators. A repetition is not necessary here. Reference is made to the reports of Barger and Dale (6), Broom and Clark (13), Clark and Broom (19), Edmunds and Hale (30), Forst and Weese (16), and the more recent work of Nelson and Pattee (1), Mendez (33), Rothlin (31) and Barger (35).

From all of this available experimental evidence it becomes readily apparent that any ergot preparation, in order to be of value for the purpose intended, *must contain significant amounts of the specific ergot alkaloids*, in a reasonably stable condition, and further, that these alkaloids must be present in defined amounts to make intelligent dosage possible. These requirements can be fulfilled only by the proper selection of methods of extraction and preparation and by employing a method for either chemical or biological standardization which will accurately estimate the alkaloidal content or physiological activity of the galenical.

THE PREPARATIONS OF ERGOT AVAILABLE TO THE PHYSICIAN.

At the present time, aside from innumerable proprietary preparations of ergot on the market, there exist two distinct types of ergot galenicals which have been accorded official recognition. The National Formulary, 5th Revision, hereafter called the N. F., recognizes a semi-solid extract prepared by extracting the drug with a chloroform water menstruum, with subsequent removal of supposedly inert material by precipitation with alcohol and evaporation of the excess menstruum at a moderate temperature. It has been designated as **Extractum Ergotae Aquosum** and is not required to be standardized in any way. In the trade it is commonly known as "ergotin" and is intended for oral administration. The U. S. Pharmacopœia, 10th Revision, hereafter called the U. S. P., recognizes "Fluidextract of Ergot," prepared by extraction of the drug with an acid-hydro-alcoholic menstruum. It is required by the U. S. P. to be physiologically standardized by the Cock's Comb Method therein described. It is suitable for oral administration only because of its acid and alcohol content and the presence of active and inert ingredients other than the specific ergot alkaloids.

THE METHODS EMPLOYED IN THE ASSAY AND STANDARDIZATION OF ERGOT PREPARATIONS.

Because of the complex chemical nature and the enormous differences in the physiological activity and potency of the active constituents of ergot and its preparations, it has been found impossible to accurately assay or standardize these preparations by chemical methods. Biological methods only can be depended upon to measure and standardize their activity. Of the numerous biological

methods which have been proposed only a few are conceded to be of value as assay methods and none of these are universally accepted. These methods, in the order of their usage or currently conceded value, are as follows:

1. The Cock's Comb Method, outlined and at present official in the U. S. P. Details of the method were published in 1927 by Gittinger and Munch (15) and in 1928 by Pattee and Nelson (28). It is reputed to measure the specific alkaloidal activity of the ergot preparation.

2. The Isolated Rabbit Uterus Method of Broom and Clark (13), and modifications (28), in which the strength of an ergot preparation is determined by the ability of the alkaloids to decrease the response of the isolated uterus of the rabbit to constant doses of epinephrine. It measures the specific alkaloidal activity of the preparations. The same principle has been applied to other tissues by Planelles (32), Rothlin (31) and others, with no particular advantages as applied to bio-assay adaptability, but of very great value in studies of the nature of ergot activity.

3. The Guinea-Pig or Cat Uterus (excised and *in situ*) Methods. These methods have been found to be of little value for ergot bio-assay purposes, because they measure the resultant effect of both the non-specific amines and the specific alkaloids (13).

4. The Pressor Methods to Cats or Dogs (13, 14, 26). These methods, though exceedingly meritorious in qualitative studies, are open to serious objections as bio-assay methods for ergot preparations because they, too, measure the resultant effect of both the amines and the alkaloids of ergot. Animal variation is also too great to permit of accurate quantitative information.

Thus, methods Nos. 1 and 2 are universally regarded as being the most accurate in estimating the clinical or specific alkaloidal activity of ergot preparations. Both have disadvantages but, in comparative studies using both methods, they have been found to yield practically identical results by Pattee and Nelson (28). Swanson (34), still more recently, reported similar results. Broom and Clark (13), Pattee and Nelson (28) and Swanson (34) agree that the Rabbit Uterus Method affords somewhat greater precision than the Cock's Comb Method but that the former is more difficult of technique and therefore requires more experience in the use of the method.

In spite of the fact that these investigators have found these two methods to be reasonably accurate in estimating the specific alkaloidal activity of Ergot preparations, the situation regarding available ergot preparations is far from being acceptable. In connection with his work in this laboratory, the author has examined by these two and other methods some hundreds of these preparations, prepared and distributed by the pharmaceutical manufacturers in both this country and abroad. This survey has revealed that statements of physiological potency and standardization upon their labels are, in fact, practically without meaning. Only a comparative few of the ampul preparations have been found to contain any alkaloidal activity whatever. The potency of the most important preparation of all, Fluidextract of Ergot, was found to vary from total inactivity up to as high as five times that specified by the U. S. P. and, to increase the gravity of the situation, the number not complying with the U. S. P. requirements was found to be vastly greater than the number of those which did. Strange to say, more were found to exceed the U. S. P. potency requirement than otherwise. A tabulation of the results of this survey will be published at a later date. The deplorable condition surrounding ergot cannot be attributed to the crude drug since none is admitted entry into this country unless it meets the U. S. P. requirements regarding potency, in addition to complying with the pharmacognostic

specifications. Obviously then, one or more of but three factors could be held responsible for the non-uniformity now existing; the unstable nature of the specific ergot alkaloids in the preparation (9), faulty extraction technique in manufacture, or, the possibility that the methods used in the biological assay and standardization of these galenicals are not accurate in all instances.

An attempt to clarify the present turbid situation has been the purpose of this investigation. Intensive studies involving the stability, nature and standardization of the various types of ergot preparations by the methods enumerated have been carried out, the results of which will be found in subsequent reports.

SUMMARY OF INVESTIGATIONS.

The following summarizes the results of the investigations:

1. The alkaloids of ergot produce bluing of the comb and wattles of cockerels, the intensity being proportional to dosage.

2. Histamine, and mixtures of the non-specific amines of ergot, produce in the absence of ergot alkaloids, a similar bluing, which is also proportional to dosage.

3. The addition of certain proportions of the amines of ergot to the alkaloids of ergot decreases the apparent potency as shown by the Cock's Comb Method. Assays by the Cock's Comb Method yield results which are too low in the case of freshly prepared fluidextracts high in amine content. After the amines are removed, the Cock's Comb test is thoroughly reliable and reasonably accurate in measuring the alkaloidal activity.

4. It is believed that histamine causes the greatest amount of interference. This amine, together with other amines and water-soluble principals, if present in sufficient quantities, as was found possible, will interfere with the assay of the ergot alkaloids by the Cock's Comb, Pressor, Guinea-Pig or Cat Uterus, or the original Broom and Clark Isolated Rabbit Uterus Methods.

5. A modification of the original Broom and Clark Method was found to yield results which were least influenced by these water-soluble amines.

6. A method has been devised which will detect and accurately measure the amine content of ergot preparations.

7. A method has been devised for the chemical removal of these interfering amines, thereby making possible an accurate estimation of the alkaloidal potency by any of the accepted bio-assay methods.

8. Extraction of powdered ergot with an aqueous menstruum removes principally amines and does not extract significant amounts of the active alkaloids. **Extractum Ergotae Aquosum** N. F. V and similar aqueous preparations, owe their activity to amines and are practically devoid of ergot alkaloids.

9. Extraction of powdered ergot with an acid hydro-alcoholid menstruum as in the U. S. P. fluidextract removes all of the amines and the alkaloids.

10. The amines were found to be less stable than the alkaloids in the menstruum of the U. S. P. fluidextract. The rapid amine deterioration results in an apparent increase in alkaloidal activity when tested by the Cock's Comb Method. The activity as shown by this method becomes stabilized after the amines have deteriorated (usually eight months or less). A slow decrease in strength then begins, depending upon storage conditions, due to deterioration of the alkaloids.

11. Regardless of variety or origin, almost every sample of ergot on the American market was found to contain an appreciable although varying amount of amine activity. A fairly large percentage contained enough amines to interfere seriously with the estimation of alkaloidal content by the Cock's Comb and other methods unless removed before assay.

The series of succeeding reports will embrace the following subjects in the order mentioned:

Part II. "A Biological Method for the Estimation of the Non-specific Amine Activity of Ergot and Its Preparations."

Part III. "A New Method for the Estimation of the Specific Alkaloidal Activity of Ergot and Its Preparations, Using the Isolated Guinea-Pig Uterus."

Part IV. "A Method for the Preparation of a Purified Fluidextract of Ergot."

Part V. "A Comparative Pharmacological Study of Crude Ergot and Fluidextract of Ergot, U. S. P. X," by:

A. The Cock's Comb Method.
B. The Isolated Rabbit Uterus Method of Broom and Clark, and Modifications.
C. The Pressor Method to Anesthetized Dogs.
D. The Isolated Guinea-Pig Uterus Method of Thompson.

Part VI. "A Pharmacological Study of Extractum Ergotae Aquosum, N. F., Fifth Edition," by:

A. The Cock's Comb Method.
B. The Isolated Rabbit Uterus Method of Broom and Clark, and Modifications.
C. The Pressor Method to Anesthetized Dogs.
D. The Isolated Guinea-Pig Uterus Methods of Thompson.

Part VII. "A Pharmacological Study of Purified Fluidextract of Ergot," by:

A. The Cock's Comb Method.
B. The Isolated Rabbit Uterus Method of Broom and Clark, and Modifications.
C. The Pressor Method to Anesthetized Dogs.
D. The Isolated Guinea-Pig Uterus Methods of Thompson.

Part VIII. "A Consideration of Standards for the Biological Assay and Standardization of Fluidextract of Ergot, U. S. P."

Part IX. "A Study of the Stability of Crude Ergot and Its Preparations: Changes Brought About by Aging."

Part X. "Discussion of Results; with Conclusions and Recommendations."

PART II. A BIOLOGICAL METHOD FOR THE ESTIMATION OF THE NON-SPECIFIC AMINE ACTIVITY OF ERGOT AND ITS PREPARATIONS.

The nature and identity of the physiologically active constituents of ergot were discussed in the first paper of this series (37). Experimental evidence shows that the ergot alkaloids are the constituents which are specific for the drug and responsible for the desired clinical effects of its preparations. The amines or amino-bases identified with the drug are regarded as being non-specific for ergot, as their presence has been found to be inconstant by Spiro and Stoll (5) and others (16). The author has found also that the non-specific amine activity of crude ergot varies enormously. Though a few samples were found to be practically free from active amines, most of those examined contained far too much amine activity to be disregarded.

A comparatively large number of amines or amino-bases, including histamine (ergamine), tyramine, acetyl and other cholines, agmatine, guanido-butylamine, and iso-amylamine, have been identified in Ergot. The literature(1, 16, 13), however, leads to a belief that only histamine, tyramine and possibly the cholines are sufficiently active, or have been shown to be present in adequate amounts to have any important share in the pharmaco-dynamic action of ergot preparations. Broom and Clark (13) have shown that the activity of B. P. Liquid Extract of Ergot is due almost entirely to the amines present, and that the U. S. P. Fluidextract of Ergot owes its activity to both groups of active principles—the alkaloids *and* the amines. Nelson and Pattee (28) state that "though no statement of the relative amounts of the two substances (histamine and tyramine) present in ergot preparations is available, it is usually accepted that more activity may be ascribed to the

histamine present than to the tyramine," because of the greater activity and occurrence of histamine.

In determining the amine activity of ergot or its preparations, it has not been found practical to use chemical methods because of the complexities encountered. Biological methods show more promise of adaptability, but results by these methods are often greatly influenced by the possible presence of the other group of active constituents—the specific alkaloids.

It is very difficult to separate quantitatively the two groups of pharmacodynamically active principles of ergot. Therefore accurate information on amine and alkaloidal activity may be obtained only by using methods that will measure the individual activity of the amine group, irrespective of the presence of the alkaloidal group, and vice versa. Up to the present time no suitable methods have been developed for the quantitative estimation of the amine activity of ergot preparations in the presence of the alkaloids, nor has a practical method been reported for the separation of the two groups of constituents, to make individual assay possible. The methods which follow were developed to supply this lack.

The biological assay methods generally used in the estimation of physiological activity of ergot and its preparations are of three general types, as follows:

(1) The Cock's Comb Method, and modifications.
(2) The Uterine Methods, with modifications:
    (*a*) Excised or Isolated, of Cats, Rabbits or Guinea-Pigs.
    (*b*) *In situ*, of Cats, Rabbits, Guinea-Pigs, etc.
(3) The Pressor Methods:
    (*a*) Systemic Circulation of Cats, Dogs, etc.
    (*b*) Pulmonary Circulation of Cats, Dogs, etc.

The Cock's Comb Method is reputed to measure the alkaloidal activity of the preparations (28, 29, 30), and is therefore of no value in estimating the amine activity in the presence of the alkaloids.

The uterus *in situ* methods measure the resultant effects of both the amines and the alkaloids (26, 13). The excised or isolated tissue methods are of two types: (1) Those in which the activity of the ergot preparation is observed directly; and (2) those in which the well-known antagonizing or vasomotor reversal effect of ergot alkaloids upon the response of the tissue to epinephrine is utilized (13, 19, 14, 28, 33, 31). In those of the first type, in which the activity of the preparation is observed directly upon the isolated uterine strips of cats or guinea-pigs, a resultant effect of the amines and alkaloids is observed, the individual constituents of both groups stimulating the tissue to contraction (1, 5, 8, 13). In those of the second type, involving the vasomotor reversal principle, the specific alkaloidal activity only is measured, as the amines do not have the the property of paralyzing the motor and inhibitory endings of the sympathetic to the action of epinephrine, the alkaloids alone being responsible for this effect (13, 31).

The Pressor Methods measure the resultant effect of all of the active principles of ergot. The alkaloids and tyramine produce a rise in blood pressure, while histamine produces a fall. The pressor effects of the amines are more transitory than those of the alkaloids, but, even so, an accurate quantitative estimation of either amine or alkaloidal activity of ergot preparations is practically impossible in many instances by this method.

Regardless of which of the pharmaco-dynamically active constituents of Ergot are responsible for the clinical activity of its preparations, all of them must be considered from the standpoint of biological assay, because it is possible for both the amines and the alkaloids to occur in sufficient amounts to manifest great activity by the currently used bio-assay methods. The author has developed a method which will measure the amine activity of crude ergot and its galenicals, irrespective of the specific alkaloidal content.

EXPERIMENTAL.

After many experiments involving the use of the various Pressor and Uterine Methods, a certain type of guinea-pig uterus was found adaptable for estimating the amine activity. Many of these biological methods have been described in the literature, but all were found to be inaccurate in the presence of the alkaloids. Using the isolated uterus of virgin guinea-pigs weighing from 200 to 300 grams, it was observed that the amines (histamine and tyramine) and the alkaloids (ergotamine and ergotoxine) all stimulated the tissue to marked contractions. In testing mixtures of these amines and alkaloids, the resultant effect of both groups was observed. In marked contrast to this observation, isolated uterine strips of large mature guinea-pigs, taken several weeks post-partem, were stimulated to contraction by the amines of ergot under certain

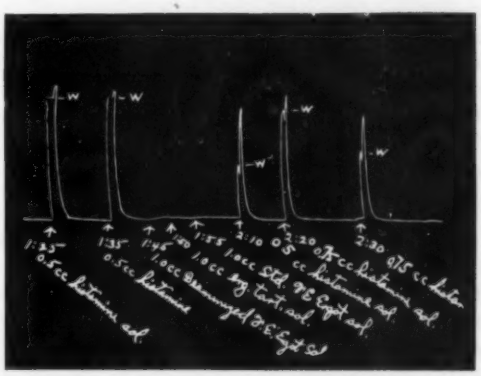


Fig. 1.—The response of the isolated uterus of the mature, non-pregnant guinea-pig to histamine and ergot alkaloids. Note the constancy of the response to histamine before the addition of the alkaloidal solutions to the baths; the ineffectiveness of the alkaloids in inducing tonic contractions; and the inhibiting influence of the alkaloids upon the histamine response.

conditions, but the alkaloids seemed to have no perceptible effect except to increase the tonus in spontaneous rhythmic contractions.

The first two contractions shown in Fig. 1 were produced by identical concentrations of histamine. Following these two contractions of equal magnitude, at 1:45 an amine-free Fluidextract of Ergot produced no contraction, although it was known to be rich in ergot alkaloids. At 1:50 a dose of ergotamine tartrate, a salt of one of the most active of the ergot alkaloids, produced no contraction. At 1:55 1.0 cc. of U. S. P. X Standard Fluidextract, dilution 1 to 5, produced no perceptible effect. Thus, the alkaloids of ergot, or preparations free from active amines but known to contain significant quantities of ergot alkaloids, failed to produce contractions of this type of isolated uterus. Figure 1 also shows the following interesting phenomenon. At 2:10, following the addition of the three alkaloidal preparations to the bath, a repetition of the original dose of histamine produced a contraction only half as great as that produced before the alkaloidal preparations were added. At 2:20 a 50 per cent increase of the histamine dose produced a contraction greater than that produced by the dose immediately preceding it, but less than that produced by the smaller dose before the strip was subjected to the action of the ergot alkaloids. Repeating the higher dose at 2:30 produced less effect than that produced at 2:20. Thus it is shown that *the alkaloids decrease the response of the isolated guinea-pig uterus of this type to histamine* in a manner analogous to the vasomotor reversal effect of ergot alkaloids upon the epinephrine response of various tissues. The indications are, therefore, that histamine acts upon essentially the same mechanism as epinephrine, although epinephrine causes the guinea-pig uterus

to relax instead of to contract. This hitherto unreported "ergot-alkaloid-histamine" reversal phenomenon has been utilized in the development of a method for the estimation of the alkaloidal activity of ergot preparations, which will be described in the third paper of this series. Pressor studies of this reversal will also be published in a later report.

As in the case of the ergot alkaloid-epinephrine reversal, the ergot alkaloids must act for some time before the histamine response is diminished. Hence the method may be utilized in the estimation of the amine activity of ergot preparations, even though the alkaloids also are present. An accurate estimation of the amine activity of crude ergot or its preparations may be obtained by observing in detail the method and procedure which follows:

METHOD.

MUSCLE.

The uteri of guinea-pigs weighing 500 to 800 grams, taken several weeks post-partem, are the most satisfactory. Uteri of smaller guinea-pigs, either nulliparous or multiparous, usually prove unsuitable, as they are often stimulated to contraction by both the amines and alkaloids of ergot. Pregnant uteri and those taken shortly after parturition are not suitable. Small, thin-walled uteri, as well as those showing diseased conditions, also must be discarded. As it is often very difficult to detect pregnancy in the animals, especially in the earlier stages, it has been found advantageous to segregate the female pigs shortly after parturition. Several weeks thereafter their uteri are usually suitable. Lactating animals are unsatisfactory. In general, the type of guinea-pig uterus best suited to this method is comparable to the type of rabbit uterus recommended for use in the Broom and Clark Rabbit Uterus Method for the estimation of ergot alkaloids (13, 28). From the larger guinea-pig uteri, eight to twelve suitable strips may be obtained, each horn being divided into two or three cross sections, which, in turn, are halved longitudinally by two parallel cuts, one directly along and one directly opposite the mesenteric attachment. The uteri may be kept on ice for three or four days in physiological salt solution, but it is best to use them before such a time has elapsed.

APPARATUS.

The apparatus is of the type usually employed for isolated tissue work, with two or more glass chambers of 50 cc. or 100 cc. capacity, mounted in a constant temperature bath, arranged to fill and empty from below. The smaller suspension chamber would save on the use of Locke's solution and would undoubtedly be fully as suitable as those of 100 cc. capacity. Those of 100 cc. capacity were used in this work. Dale and Laidlaw (20), Smith and McCloskey (21), and Pattee and Nelson (28), describe this apparatus in greater detail.

METHOD FOR ESTIMATING NON-SPECIFIC AMINE ACTIVITY.

The similar uterine strips are suspended, one pair at a time, in separate chambers in oxygenated Locke's solution at 38° C. and arranged to record on a slow-moving kymograph in the usual manner. The tension on the strip is important, and can be determined by experience only. A dose of histamine which will produce a pronounced, but submaximal contraction for each strip is then determined. When the strips, after several trials, are found to produce contractions of constant submaximal magnitude from a given concentration, at a constant time interval between doses, the amine activity of the ergot preparation is ascertained by comparison. After each dose the strips are washed and the chambers refilled with Locke's solution. The use of two strips provides a check as well as a time-saving factor. If appreciable quantities of ergot alkaloids are present in the unknown, as is invariably the case in Fluidextract of Ergot, the first trial of the unknown on each strip is all that may be considered significant, because any alkaloids present diminish the amine response. If a certain sub-maximal dose continues to give constant contractions, as is often the case with aqueous extracts, it is indicated that active ergot alkaloids are not present. The amine activity is expressed in terms of histamine.

It is absolutely essential that all doses be added to the baths at definite time intervals. Exactly 10 minutes between each dose has been found satisfactory in most instances, although some uteri will contract and relax sufficiently in a shorter time. Whatever time interval is used, it must remain constant between each dose throughout the assay. Figure 2 shows the constant response to graded dosages obtained when a definite time interval is carefully observed.

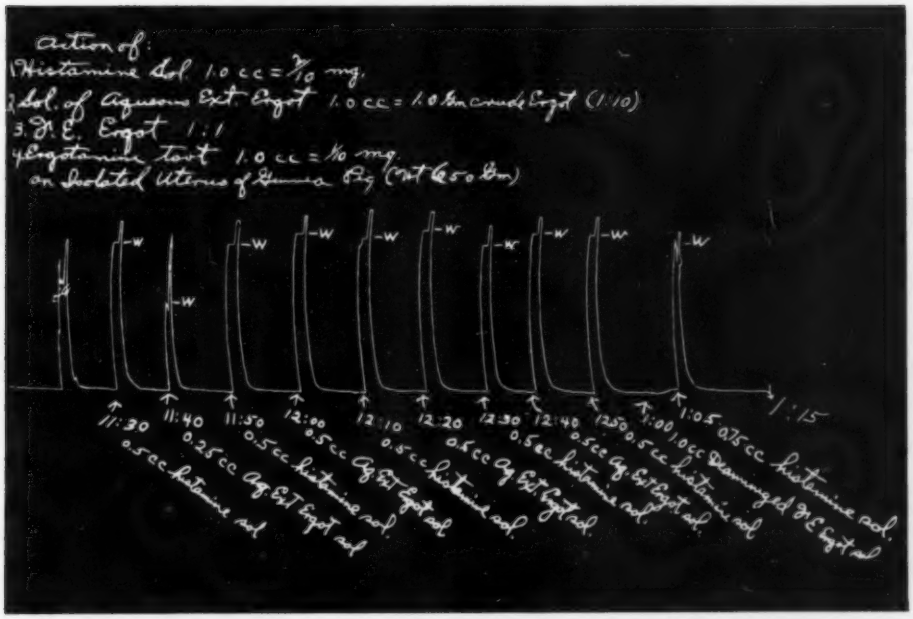


Fig. 2.—A determination of the non-specific amine activity of an ergot preparation by the isolated guinea-pig uterus method described. Note the constancy of the response to histamine and the ergot preparation until 12:50; showing the absence of ergot alkaloids but a pronounced amine activity. Note also the absence of response to the amine-free alkaloidal ergot preparation at 1:00, and the inhibiting influence of this alkaloidal preparation upon the response of the uterus to the increased dose of histamine at 1:05. The "W" indicates wash.

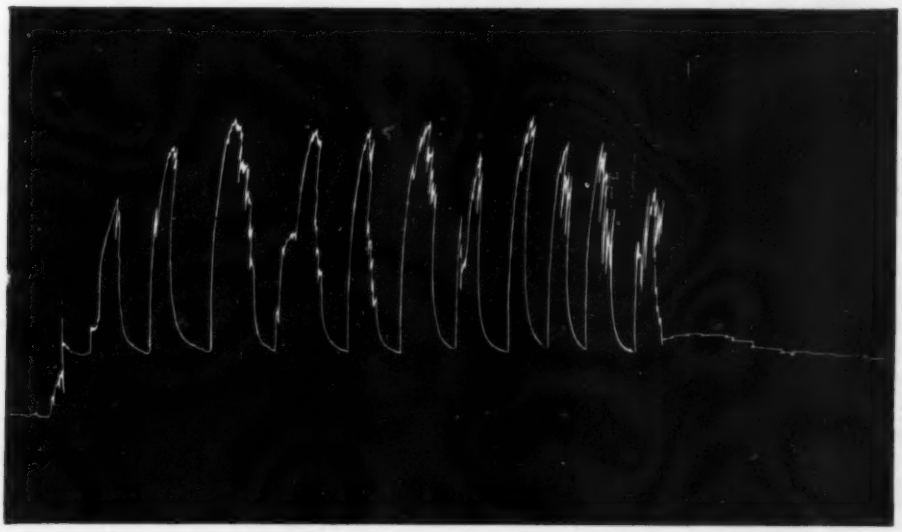


Fig. 3.—The variable response of the guinea-pig uterus to constant doses of histamine observed when an improper tension on the strip is used. The tension employed is of paramount importance.

The weighting of the levers is of paramount importance. It is impossible to state the amount of tension to be employed, as each strip will differ in this respect. In general, the levers must be weighted sufficiently to obviate appreciable spontaneous rhythmic contractions, but not so heavily as to cause symptoms of fatigue in the muscle. When the strips are found to react according to the dose added to the bath, and *constantly* to a given dose, they are ready for assay purposes.

If insufficiently weighted, the magnitude of contraction will not distinguish between varying doses. If weighted too much, the magnitude of contraction diminishes with each succeeding dose, when the doses are constant, or even when the dose is increased. Figure 3 shows the irregular response of a strip to constant dosage of histamine when improperly weighted.

The following is the composition of the Locke's solution that has been used in this work:

	Grams.
Sodium chloride	9.0
Potassium chloride	0.42
Magnesium chloride	0.005
Calcium chloride	0.24
Sodium bicarbonate	0.50
Dextrose	0.50
Glass-redistilled water to make	1000 cc.

This Locke's solution is freshly prepared each day from stock solutions of 20-fold concentration, exclusive of the sodium bicarbonate and dextrose. The sodium bicarbonate and dextrose are weighed out each time as required.

The oxygen used is passed through an aqueous 4 per cent sodium bicarbonate solution, and then conducted to the tissue chambers, where it is evolved through the Locke's solution surrounding the tissue. The rate is kept at approximately 20 bubbles per minute.

DETERMINATION OF NON-SPECIFIC AMINE ACTIVITY OF CRUDE ERGOT: PREPARATION OF TEST EXTRACT.

Grind the crude ergot and de-fat or de-grease as directed in the U. S. P. for Fluidextract of Ergot. A 50-gram portion is convenient. After the benzine odor has left the drug, add enough 10 per cent sodium bicarbonate solution to render the powder evenly and distinctly moist and to keep it so during 2 to 4 hours' maceration in a refrigerator. Then pack the moist drug loosely in a small glass percolator provided with a glass stop-cock. Add cold distilled water to the percolator, and, when the liquid begins to drop from the lower orifice, interrupt percolation and let maceration proceed for an additional 6 hours in a refrigerator. Allow the percolation to proceed at a rate of 15 drops per minute until a small portion directly from the percolator is found to be inactive on the guinea-pig uterus by the method previously described.

The amine activity of crude ergot, as well as the rate of extraction of the drug, varies enormously. It is therefore practically impossible to specify the amount of percolate to be obtained. All operations must be carried out at refrigeration temperature and the percolate must be stored in a refrigerator until the assay has been completed. At higher temperatures fermentation and putrefaction develop, resulting in increased amine activity. The percolate or aqueous extract thus prepared wil be found to be practically devoid of active ergot alkaloids.

Knowing the volume of percolate collected from the specified amount of drug used in the assay, determine the amine activity by the guinea-pig uterus method described, expressing the result in terms of milligrams of histamine per gram of ergot or as the percentage of amine activity in terms of histamine.

Figure 2 shows an example of the estimation of the amine activity of a crude ergot by the methods described. Note that the uterine strip is shown to be unresponsive to the alkaloidal preparation at 1:00. After the alkaloidal dose, however, a 0.75-cc. dose of histamine solution at 1:05 produced a contraction no greater than the 0.5-cc. dose originally produced, showing partial paralysis of the uterine strip by the alkaloids to the effect of histamine.

DETERMINATION OF NON-SPECIFIC AMINE ACTIVITY OF SOLID, SEMI-SOLID OR LIQUID AQUEOUS EXTRACTS OF ERGOT.

Triturate an exact weight of the solid or semi-solid extract in a glass or agate mortar with a definite amount of Locke's solution (1:25 is a convenient concentration) until the extract is dispersed. (This applies only to the solid or semi-solid extracts, the others already being in a state of solution.) Carefully but completely neutralize any acidity by the cautious addition of

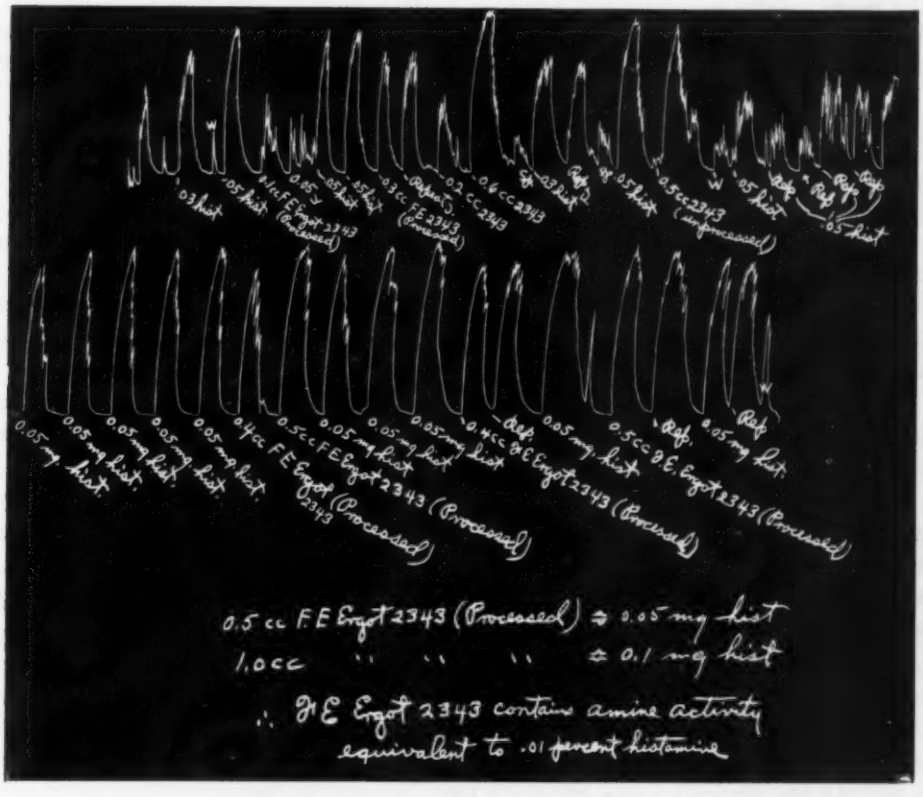

0.5 cc F.E Ergot 2343 (Processed) ≑ 0.05 mg hist
1.0 cc " " " ≑ 0.1 mg hist
∴ F.E Ergot 2343 contains amine activity
equivalent to .01 percent histamine

Fig. 4.—The response of two similar strips of isolated guinea-pig uterus. The upper tracing shows the effect of histamine and a Fluidextract of Ergot before and after being processed according to the method described. Note the constancy of response to the processed Fluidextract in varied doses as compared to the inhibited response to histamine after the unprocessed Fluidextract was added. The inhibition was produced by the interfering alkaloids present in the unprocessed preparation. The lower tracing shows a typical estimation of the non-specific amine activity of the same U. S. P. Fluidextract by the method recommended. Note the absence of alkaloidal interference as shown by the constant response to both the histamine standard and the processed Fluidextract.

powdered sodium bicarbonate, and filter. Do not bring up to volume by adding more Locke's solution after filtration.

Determine the amine activity by the guinea-pig uterus method as described for crude ergot. Results are conveniently expressed as percentage of amines calculated as histamine. The amine activity of all ergot preparations varies greatly. In determining this activity, the doses and concentrations must be varied according to the activity found. No alkaloidal interference should be encountered if this method is carefully followed.

DETERMINATION OF NON-SPECIFIC AMINE ACTIVITY OF FLUIDEXTRACT OF ERGOT AND OTHER ALCOHOLIC PREPARATIONS OF ERGOT.

Pippette 10 cc. of the preparation into a small beaker and dealcoholize by using a warm-air blast (a barber's hair dryer serves admirably). Carefully neutralize any acidity by the cautious addition of powdered sodium bicarbonate. Bring up to the original volume with Locke's solution, mix thoroughly and filter.

Determine the amine activity by the guinea-pig uterus method as directed for crude Ergot. The amine activity is conveniently expressed in percentage, calculated as histamine. These preparations will also be found to vary enormously in active amine content, some being devoid of such activity while others contain more than the equivalent of one milligram of histamine per cubic centimeter of preparation. Figure 4 shows an assay of the amine activity of a sample of U. S. P. Fluidextract of Ergot. Note the absence of alkaloidal interference, shown by the constancy of the magnitude of contraction to graded dosage of the processed preparation.

SUMMARY.

A type of guinea-pig uterus is described which, under specified conditions, is stimulated to contraction directly by the non-specific amines of ergot, but is not so affected by the specific ergot alkaloids. The alkaloids increase the tonus in rhythmic contraction of the muscle, but do not stimulate prompt tonic contractions directly.

The alkaloids of ergot were found to inhibit the response of the guinea-pig uterus to histamine in a manner analogous to the well-known vasomotor reversal relation between ergot alkaloids and epinephrine upon various tissues.

A method is described for the estimation of non-specific amine activity of ergot and its preparations, including methods for the preparation of the test solutions which largely obviate alkaloidal interference. Histamine was used as the standard for comparison because it is responsible for the greater amount of the amine activity of ergot, and, further, because it is readily available.

PART III. A METHOD FOR THE ESTIMATION OF SPECIFIC ALKALOIDAL ACTIVITY OF ERGOT PREPARATIONS UPON THE ISOLATED UTERUS OF THE GUINEA-PIG.

The recent literature on ergot leads to a belief that the specific alkaloidal activity of ergot is due to ergotamine and ergotoxine and that these two alkaloids are identical as to pharmacological and clinical action, although they differ somewhat in chemical structure and physiological potency (13, 1, 28).

The chemical studies of Kraft, Tanret, Barger and Stoll have made these alkaloids available in the pure state. By the successful isolation of these alkaloids of ergot, pharmacological and clinical studies on them were made possible. The reports of these studies tend to establish that the ergot alkaloids are specific for the drug and responsible for the desirable clinical effects of ergot preparations, while the amines (histamine, tyramine, etc.) are non-specific and therefore relatively unimportant from the clinical standpoint.

Because of the great amount of experimental evidence thus set forth, the present tendency in the biological assay and standardization of ergot preparations is to employ methods that measure the specific alkaloidal activity, disregarding

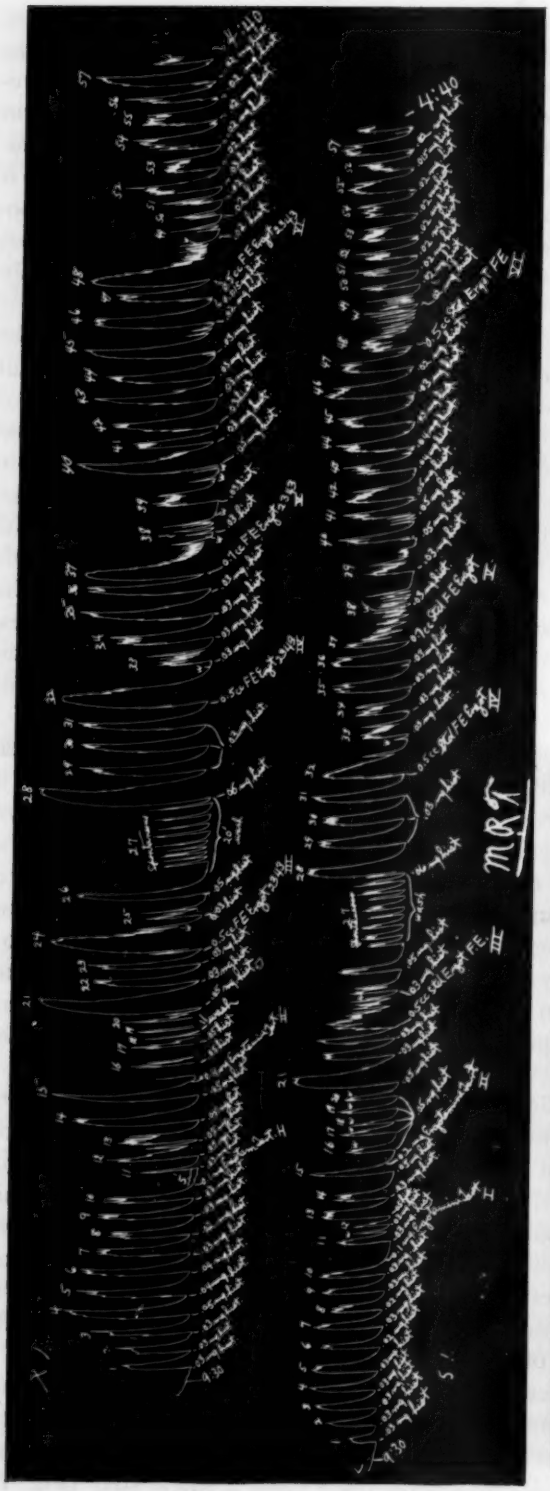
completely the presence of the non-specific amines. Just what part the amines, such as histamine and tyramine, play in the clinical activity of ergot preparations is not definitely known, although histamine, the most important of them, is reported to be practically without effect when administered orally (14) at least in the amounts ordinarily found in these preparations. Both histamine and tyramine manifest great activity when administered hypodermically, however, and it is possible that they play a part in the action of preparations intended for hypodermic use. It is generally known that the ergot alkaloids are effective *both orally and hypodermically* and that they are specific for the drug, thereby establishing their greater importance.

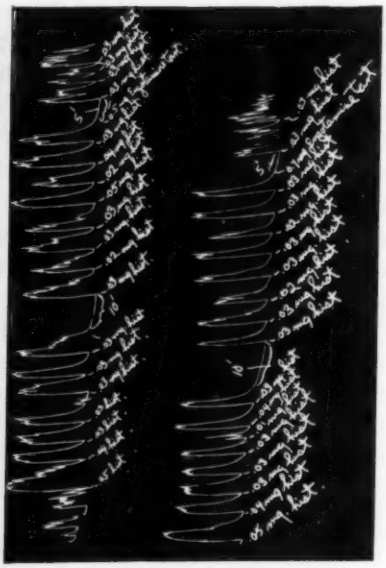
Of the many methods proposed for the biological standardization of the specific alkaloidal activity of ergot preparations, only two have shown sufficient reliability in application to warrant general recognition. These are the so-called Cock's Comb test, official in the U. S. P., and the Isolated Rabbit Uterus Method of Broom and Clark (13). Pattee and Nelson (28) found these two methods to yield practically identical results in estimating the alkaloidal activity of ergot preparations. Broom and Clark (13) were unable to get accurate results by the Cock's Comb Method because of variation in susceptibility of cocks. Edmunds and Hale (30) found the Cock's Comb Method to be reasonably accurate. In the writer's experience, the two methods yield comparable results in most instances, but great variations were observed in some cases. The results obtained in comparative studies of these two and other methods will follow in other papers of this series.

A method for the estimation of the specific alkaloidal activity of ergot preparations has been developed which, it is believed, is worthy of consideration, since it clearly shows the difference between the amine and alkaloidal activity of ergot upon the isolated uterus of the guinea-pig. This method is comparable to the Isolated Rabbit Uterus Method of Broom and Clark (13), with the exception of the smooth muscle employed and the substance used for stimulating the tissue to contraction. Bio-assayists experienced in the use of the Rabbit Uterus Method have found considerable difficulty in obtaining rabbits of the type necessary, as pointed out by Pattee and Nelson (28) and Swanson (34). Guinea-pigs are comparatively plentiful and are cheaper than other experimental animals suitable for the purpose. The uterus of the guinea-pig is utilized in the new method.

The well-known "ergot alkaloid-epinephrine reversal" cannot be applied to the guinea-pig uterus because epinephrine causes relaxation instead of contraction of this tissue. It has been shown that a similar relation exists between the ergot alkaloids and histamine (Part II). Histamine was shown to cause definite tonic contraction of strips of isolated guinea-pig uterus of a specified type. This contraction could be inhibited or abolished by allowing the ergot alkaloids to act upon the tissue for a short time. A certain definite concentration of ergot alkaloids is required to produce this inhibition or reversal and therefore this reaction can be utilized to estimate the quantity of alkaloidal activity in ergot preparations.

The method has two distinct advantages over the Isolated Rabbit Uterus Method. Suitable guinea-pigs are more readily available than suitable rabbits, and the uterine strips of the guinea-pig recover from the effects of the ergot alkaloids rather quickly, thereby permitting several trials upon a single strip (Fig. 7).





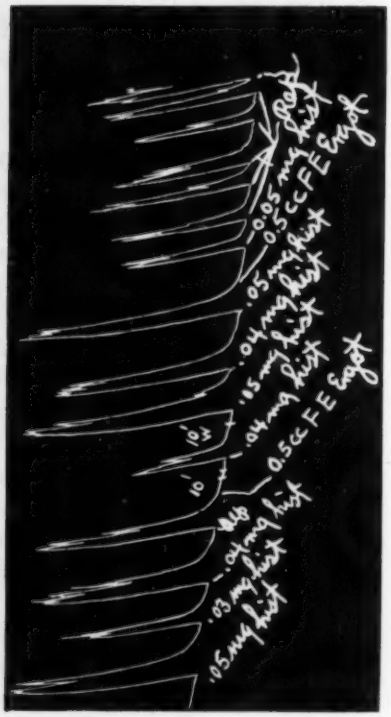


Fig. 5, below, Fig. 6, below, on right. Fig. 7, top. For legends see next page.

Fig. 5.—The response of the isolated guinea-pig uterus to histamine, and a U. S. P. Fluidextract of Ergot which was practically devoid of amine activity. The Fluidextract is shown to contain sufficient alkaloidal activity to appreciably inhibit the normal response to histamine.

Fig. 6.—Showing the constant response of similar strips of isolated guinea-pig uterus to histamine up to the point of the administration of ergotamine tartrate. By permitting this alkaloid to act upon the strips for five minutes, the response to histamine was appreciably inhibited in each case.

Fig. 7.—The upper and lower tracings show the response of a single pair of similar strips of guinea-pig uterus. The first few contractions of each strip illustrate the necessity of repeating the doses of histamine until constant response to a given concentration is obtained. Following this, each strip was subjected to six different applications of alkaloidal ergot preparations during a period of over seven hours.

In each instance the alkaloids were permitted to act for a time sufficient to cause a definite inhibition of the histamine response. Recovery from the alkaloidal effect can be noted after each application. The strips were functioning satisfactorily when the experiment was discontinued at the end of seven hours.

THE ERGOT ALKALOID-HISTAMINE REVERSAL.

The first evidence of this reversal was observed in pressor studies of ergot preparations. This led to the supposition that it should be possible to produce further evidence of such a reversal upon uterine muscle. Experimental results (Part II) show the inhibitory action of ergot alkaloids upon the response of the isolated guinea-pig uterus to histamine or ergot amines. Broom and Clark (13) in their Fig. 4, actually show this reversal relation between ergot alkaloids and amines upon the isolated guinea-pig uterus, although they offer an explanation with which the writer does not entirely agree. They show the effect of a B. P. Liquid Extract upon one horn and of a U. S. P. Fluidextract of Ergot upon the other horn of the isolated uterus of the same guinea-pig. The response of the muscle to the B. P. extract remained constant "because it depends entirely on the histamine content." The writer agrees that this preparation contains practically no active alkaloids, but, because of experimental pressor studies, believes that the activity is due to a mixture of amines rather than to histamine alone, although histamine is the most active and predominating amine regarding activity. The response of the muscle to U. S. P. Fluidextract of Ergot, in the same illustration, "becomes less on repetition because it depends largely on the alkaloidal content of the ergot." This, in the writer's experience, is true only in part. Since, as Broom and Clark state, both of these preparations were made from the same batch of ergot, each should contain comparable quantities of active amines. The B. P. and U. S. P. processes of manufacture, if the same batch of drug is used in each, yield preparations which are similar with respect to amounts of non-specific amine activity, differing only in the specific alkaloidal content. The U. S. P. Fluidextract always contains more of the alkaloids than the B. P. preparation. This has been shown repeatedly by the writer. Broom and Clark (13) explain the diminishing response from the repeated administration of the U. S. P. Fluidextract to the isolated uterus of the guinea-pig as follows: "* * * the amines present in ergot produce an effect as great or greater than that produced by the ergot alkaloids. The ergot alkaloids, moreover, can only excite the uterus once and after the first application of ergotamine the uterus will not respond to a second administration although its excitability to histamine is unaltered. The ergot extracts were found to vary as regards the constancy of the reaction they produced; submaximal doses of the B. P. preparations produced constant response repeatedly, whereas with submaximal doses of the U. S. P. preparations the first application produced the greatest response. This effect is shown in Fig. 4. Apparently in the case of the U. S. P. preparations about half the action on the guinea-pig's uterus is due to its alkaloidal content and about half to its amine content. In the case of the B. P. preparation the whole action is due to its amine content."

These investigators do not state the type of guinea-pigs used in their work. Experiments involving different types of guinea-pig uteri definitely show that this is a vital factor. The isolated uteri of young, immature guinea-pigs usually are stimulated to contraction by both the alkaloids and the amines of ergot, histamine being decidedly most active in this respect. The

resultant effects of mixtures of alkaloids and amines were found to be similar to that described by Broom and Clark (13) for U. S. P. Fluidextract of Ergot. If the isolated uteri of larger, mature guinea-pigs are employed, however, the contractions produced are due almost entirely to the amines present. In the case of B. P. Liquid Extract or the N. F. V. Aqueous Extract, constant response of the tissue is observed because the activity of these preparations depends almost entirely upon the amine content. Fluidextract of Ergot contains all of the amines and alkaloids that were present in the parent drug. The first application of this preparation to the uterine strip results in a contraction whose magnitude depends upon the amine content of the fluidextract. Upon repetition of the application the response diminishes, the lessening of the response depending upon the proportion of alkaloids and amines present and the time the preparation is permitted to act upon the tissue before replacing the poisoned Locke's solution with fresh Locke's solution. This diminishing effect is shown in Fig. 1, Part II of this manuscript, and is explained by the "ergot-alkaloid-histamine" reversal therein described. This consists essentially in the ability of ergot alkaloids to inhibit or abolish the response of the guinea-pig uterus to histamine or ergot amines in a manner analogous to the well-known "ergot-alkaloid-epinephrine" reversal upon the rabbit uterus.

The utilization of the "ergot-alkaloid-histamine" reversal upon the guinea-pig uterus in estimating the alkaloidal activity of ergot preparations would at first seem impossible, as all of these preparations usually contain variable quantities of histamine as well as other amines. Therefore, when the ergot preparation is applied, the presence of histamine or other amines of ergot would increase the ultimate amine concentration of the bath, causing an abnormally great contraction of the uterus when the histamine effect was observed after the alkaloids had exerted their definite inhibiting effect. Experimental studies have shown that the natural amine content of ergot preparations causes no greater interference in this method than in the Rabbit Uterus Method, in which the test contraction is induced by epinephrine. The amine interference is obviated in this Isolated Guinea-Pig Uterus Method in the same way that the same interference is obviated in the Isolated Rabbit Uterus Method as modified by Pattee and Nelson (28). These investigators state that by sufficient washing of the strip of rabbit uterus after the ergot preparation has acted upon it for a definite length of time, but before the final epinephrine response is observed, the interfering amines are removed, thereby permitting the epinephrine to produce its true alkaloid-inhibited response. They also show definitely that the amines may be present in amounts sufficient to increase the ultimate epinephrine response if the washing technique is not observed. By observing the same technique the amine interference is obviated in the Guinea-Pig Uterus Method also.

METHOD.

The method is based upon the ability of the active alkaloids of ergot to inhibit or abolish the response of the isolated guinea-pig uterus to histamine (Fig. 5) in a manner analogous to the "ergot alkaloid-epinephrine" reversal principle utilized in the Isolated Rabbit Uterus Method of Broom and Clark (13). The method is carried out in the same manner as the Broom and Clark Isolated Rabbit Uterus Method (13, 28) except that similar strips of guinea-pig uterus are used instead of similar strips of rabbit uterus, and histamine is used instead of epinephrine to induce the contractile response.

APPARATUS AND MUSCLE.

The apparatus, Locke's solution, and smooth muscle employed in this method are the same as those used in the method described for the estimation of the non-specific amine activity of ergot and its preparations (Part II).

TECHNIQUE.

The uteri are obtained from mature guinea-pigs weighing from 500 to 800 grams, taken several weeks post-partem. Segregation of proper animals immediately after parturition largely obviates obtaining unsuitable uteri. The animal is killed by a blow on the head and the uterus is carefully dissected out in the usual manner, removing fallopian tubes, ovaries, etc. From the larger uteri, eight to twelve suitable strips may be obtained, each horn being divided into two or three cross sections, which, in turn, are halved longitudinally by two parallel cuts, one directly along and one directly opposite the mesenteric attachment. These strips are immersed in physio-

logical saline solution and kept on ice. In this condition they may be kept for 3 or 4 days, but it is preferable to use them before so long a time has elapsed. It has been the practice of the writer to make but one of the longitudinal cuts along each cross section before the section is to be used. When the section is to be used the other cut is made, dividing the section into two similar strips. This insures the use of similar, instead of dissimilar, strips.

Two similar strips are then mounted in separate chambers of the apparatus and arranged to record in the usual manner. The tension used is of paramount importance. It must be sufficient to produce relaxation and prevent appreciable spontaneous rhythmic contractions but not so great as to prevent a good contraction or cause the strip to show symptoms of fatigue (as evidenced by a diminishing response to a constant dose of histamine) in repeated application of histamine. Each strip used is a problem unto itself in this respect. The tension to be used can be determined only by experience. When properly weighted the spontaneous contractions are not in evidence, but a prompt contraction is produced by the addition of a proper concentration of histamine. The poisoned Locke's solution is replaced with fresh solution after each dose as soon as the maximum amplitude of the contraction is attained.

As shown in Fig. 7, the response of the strips to constant doses of histamine usually increases during the first few trials. In the writer's experience it is of advantage to let the strips stand for half an hour before testing their response to histamine. The response will then be more constant than it would if histamine were introduced immediately after mounting. The dose of histamine which will produce a pronounced but submaximal contraction is then determined by trial. This dose is repeated until the response of the strip becomes constant. After waiting twenty minutes, the constancy is again observed. Having thus determined the dose necessary and the constancy of response to this dose, the strips are in readiness for testing the alkaloidal activity of the ergot preparation.

The standard, which may be either the U. S. P. Standard Fluidextract supplied by this laboratory or a solution of one of the specific alkaloids, is added to one bath and the preparation to be tested is added to the other. In each case, the time of the addition of each is accurately recorded. At this point an indication of the non-specific amine activity of the preparation may be obtained. If the amine content is low, a low contraction will result; if high, the contraction will be correspondingly great. Occasionally preparations will be found to contain enough amines to cause a maximal contraction when they are added to the bath (Fig. 7). In any case, however, the strip gradually relaxes. The ergot preparation is allowed to act on the strips exactly fifteen minutes in each case, after which the strips are washed. After another three minutes the previously determined dose of histamine is repeated. When its effect has been obtained it is washed off and in a few minutes repeated as a check, all factors being carefully kept identical for each strip. Similarly, at definite time intervals of a few minutes, the effect of further repetitions of the same histamine dose is observed. The potency of the preparation is determined by a comparison of the percentage inhibition produced by the unknown with the percentage inhibition produced by the standard in a manner identical with that recommended by Pattee and Nelson (28) in carrying out the Broom and Clark Method. The dose of ergot should be sufficient to reduce the histamine response 25 to 50 per cent. Further reduction is hardly significant, as spontaneous rhythmic contractions of low magnitude frequently develop, making the exact inhibition difficult to determine. After several washings the uterus soon recovers from the effect of the ergot alkaloids. When the histamine response again becomes constant, as it usually does within half an hour, another trial of the ergot preparation may be made. The effect of the repetition of application of ergot alkaloids and recovery of the similar strips of guinea-pig uterus is shown in Fig. 7. In this experiment the effects of six different trials with alkaloidal ergot preparations were observed over a period of more than seven hours, at the end of which time each strip was still functioning satisfactorily.

It will be noted in the illustrations that much higher concentrations of ergot alkaloids are necessary to appreciably inhibit the histamine response of the guinea-pig uterus than are required to diminish the epinephrine response of the rabbit uterus. The inhibition of the histamine response depends upon two factors, the concentration of ergot alkaloids employed and the length of time the alkaloids are permitted to act upon the strips. In general, the concentration of the ergot alkaloids employed bears an inverse relation to the time of action necessary to produce a definite inhibition. Therefore, increasing the time of alkaloidal action from 5 or 10 minutes

(as used in the Broom and Clark Method) to 15 or 20 minutes permits the effective concentration of ergot alkaloids to be lowered.

It is impossible to state the concentration of ergot alkaloids or of histamine to be employed because of the variations in uteri. The illustrations give approximate indications of concentrations when 100-cc. tissue baths are used, although in these experiments the time interval used was varied. Table I shows typical results obtained in an assay:

TABLE I.—RESULTS OBTAINED FROM SIMILAR STRIPS OF THE SAME GUINEA-PIG UTERUS.

	Commercial sample Fluidextract of Ergot No. 6.		Standard Fluidextract of Ergot.	
Trial no.	Dose (in 100-cc. baths). Cc.	Inhibition, per cent.	Dose (in 100-cc. baths). Cc.	Inhibition, per cent.
1	0.5	>60.0	0.5	40.6
2	0.25	42.1	0.5	44.2
3	0.25	44.7	0.5	46.6
4	0.2	35.8	0.5	44.5
5	0.15	<30.0	0.5	47.2

> More than. < Less than.

The results in Table I show that 0.25 cc. Fluidextract No. 6 is approximately equivalent to 0.5 cc. of Standard Fluidextract Ergot. In other words Fluidextract Ergot No. 6 is approximately twice the strength of the Standard.

The results obtained by this isolated Guinea-Pig Uterus Method agree in most instances with those obtained by the Cock's Comb and the Broom and Clark Rabbit Uterus Methods. Comparative studies of these three methods will be given in another paper of this series.

SUMMARY.

Studies involving the use of the isolated uterus of the mature, non-pregnant guinea-pig have shown that the specific alkaloids and the non-specific amines of ergot act in a decidedly dissimilar manner. The pure alkaloids increase the tonus in rhythmic contractions but are relatively ineffective in stimulating prompt tonic contractions. The non-specific amines (histamine and aqueous extracts of ergot containing essentially nothing but histamine, tyramine, etc.) are very active in inducing prompt tonic contractions. The tonic contractions produced by histamine or mixtures of the non-specific amines of ergot can be inhibited or abolished by permitting the specific ergot alkaloids to act upon the muscle for a time.

It was observed further that the inhibition of the amine response of the isolated guinea-pig uterus by the ergot alkaloids depended upon the concentration of ergot alkaloids used and the time the alkaloids were permitted to act.

The method for the estimation of alkaloidal activity of ergot preparations here described depends upon this "histamine-ergot alkaloid" relationship upon the isolated guinea-pig uterus.

(*To be continued*)

ABSTRACT OF PAPER, SCIENTIFIC SECTION.

"Studies of the Analysis and Chemistry of Neoarsphenamine. II. Studies on the Chemistry of Sodium Formaldehyde sulphoxylate and Their Relation to the Structure of Neoarsphenamine," by A. E. Jurist and W. G. Christiansen.

The stability and reactions of sodium formaldehyde sulphoxylate in acid and alkali have been studied and its structure derived from these results. Thus the structure of Neoarsphenamine has been developed and the existence of at least two, and perhaps three tautomeric forms is indicated.

COMMENTS ON THE PAPER ON BIOLOGICAL STANDARD FOR ERGOT PRESENTED BY MARVIN R. THOMPSON, AT THE RAPID CITY MEETING OF THE A. PH. A.*

BY H. H. RUSBY,[1] M.D.

Since September of 1927, I have been engaged in securing the application of the U. S. P. biological test to a large number of samples of ergot and Fluidextract of Ergot. The methods followed in this work have been such that the tests have been quite as much tests of the method of testing as of the samples of ergot employed, and I feel that the results have an important bearing on the question raised in Mr. Thompson's paper.

It is to be noted that I have not in any case applied this test myself, so that personal prejudice is quite impossible. However, in very few cases has the analyst making the test had any knowledge as to the source of the sample, which has been supplied through a third party. In almost every case, the same sample has been referred to more than one analyst, in several cases to three and in one case to four. Again, the same sample has gone to the same analyst more than once, without his knowledge that he had previously tested it. It will thus be seen that the samples and the tests have depended for the results, solely upon their own merits.

Under these conditions, I have received the following reports of relative therapeutical strength, by percentage, exact conformity with the U. S. P. test being regarded as indicating 100 per cent. The reports, on the same lot of ergot, thus referred to different analysts and to the same analyst at different times, are as follows: "90.9%–100%–110%–112%–123%–133%–155%–165%–167%. Not all of these figures referred to the same lot of fluidextract, although all the fluidextracts were made from the same lot of ergot.

Equally discordant reports have been received from portions of fluidextract taken from the same bottle. Thus, three such samples were sent for comparison to two different analysts. One reported 128%, 130% and 125%, the other reported 166%, 166% and 250%.

Of two other samples sent to the same analyst, one reported 125% and 167%, the other 155% and 125%. It happened that one of my samples was submitted by Chairman Cook of the Revision Committee to some official at Washington. Regarding the results of this test, Professor Cook has told me that "it showed 100%, the same as the others." I took the precaution to send this sample to two analysts who reported 128% and 168%. Another sample that has been reported in a printed article as being of 195% to 200%, the identity of the sample not being stated, I believe to be the same as the one above referred to.

From this experience of two years, involving a large number of samples, I feel sure that the Cock's Comb test cannot be regarded as capable of yielding reasonably uniform results in the hands of different analysts, or of the same analyst at different times.

It is also true that any sub-standard fluidextract can be caused to meet and ex-

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* Scientific Section, A. PH. A., Rapid City meeting, 1929.

[1] The author of these comments was not able to be present at the reading of Mr. Thompson's paper, but Mr. Thompson was kind enough to inform him of the general subject as presented.

ceed the biological requirement by the addition to it of a minute amount of some substance that cannot be detected by the analyst.

Another conclusion regarding the value of this test is justified by the following experience.

A lot of ergot, stored in bags in a warehouse, was thoroughly watersoaked in the extinguishing of a fire that occurred in that warehouse. After lying in this condition in a damp basement for three weeks, this ergot was examined by three arbitrators, in order to fix the amount of damage, for the fire underwriters. At this time, the ergot was still thoroughly watersoaked, a mass of mould, emitting a very offensive and rancid odor, thoroughly decolorized on the surface and to a great extent internally, many of the grains being soft and mushy, and there being extensive decomposition of the fat and proteid matter, and supposedly also of the alkaloids. The ergot was unanimously voted unfit and dangerous for use and was written down as a total loss. Nevertheless, samples of this ergot that I had submitted to biological test by two pharmacologists were reported as having 125% and 167% of the official strength.

From this and many similar experiences, I conclude that the Cock's Comb test will indicate perfect quality in an ergot that is badly decomposed and unfit for use.

Another fact that I have long known and which has been confirmed by these experiments is that no necessity whatever exists for the Cock's Comb test in its present form, even assuming that it was reliable. It is not often that a sample of ergot, that any competent judge of the drug would accept as being of fair quality, is found deficient by the Cock's Comb test, but I have known a great many that any competent judge would condemn as unfit for use that were indicated as of good quality by this test. Indeed, if there is any conflict between a judgment based on physical examination of the drug and the result of the Cock's Comb test, then I am prepared to say that it is the test that is at fault.

The only value of this Cock's Comb test, and the only actual use that has been made of it, is to secure the approval of ergot that is not entitled to confidence, and to prevent the retail pharmacist from supplying fluidextract of his own manufacture. This should be denominated abuse, rather than use! It will doubtless interest this audience to know that on one occasion, after I had lectured to my students on the subject of ergot, I advised them that the most certain method by which they could supply a perfect fluidextract of ergot was to carefully select the drug according to the instruction received in our class in pharmacognosy and to make their own fluidextract by the process taught them with equal care in the department of pharmacy. After the lecture several of them came to me and reminded me that the requirement of the biological test made it impossible for them to dispense the drug of their own manufacture, as they had no means of applying this test. My answer was that they would be perfectly justified in dispensing such a fluidextract without the formality of making the test.

"An Empiric Assay for Compound Pills of Mercurous Chloride," by L. E. Warren.

Jenkins method for assay of podophyllum determines resins and certain vegetable acids together. Each vegetable ingredient of compound cathartic pills studied separately by this method. Ten commercial samples analyzed. Addition of resin of jalap, resin of ipomoea or aloes readily detected by this method.—Scientific Section, A. PH. A.

THE STANDARDIZATION AND STABILIZATION OF ERGOT PREPARATIONS.*

THE STUDY OF BIOLOGICAL METHODS OF ASSAYING ERGOT PREPARATIONS AND THE HYDROGEN-ION CONCENTRATION FACTOR.

A Preliminary Report—Paper VII.

BY EDWARD E. SWANSON.[1]

1. Introduction
2. Methods of Assay
3. The Selection of a Muscle
4. Technique of Assaying
5. Experimental Data
6. Ergotoxine and Ergotamine Relationship
7. Summary

1. INTRODUCTION.

The principle constituents of ergot are considered to be ergotoxine, ergotamine, tyramine, acetylcholine and histamine. Ergotoxine and ergotamine, however, are the only constituents that will produce the characteristic cyanotic and gangrenous comb of the cock.

Numerous methods of assaying ergot have been studied and reported, but only two or three methods show agreement as to relative values. Some of the methods reported are:

(*a*) the Isolated Guinea-Pig Uterus Method,
(*b*) the Blood Pressure Method,
(*c*) the Vasomotor Reversal Method (Barger & Dale) (1),
(*d*) the Cat's Uterus *in situ* Method,
(*e*) the Cock's Comb Method U. S. P. (Edmunds & Hale) (2),
(*f*) the Isolated Rabbit's Uterus Method (Broom & Clark) (3).

Edmunds and Hale (2) found that the Cock's Comb Method and Guinea-Pig Uterus Method are in close agreement in measuring the activity of ergot, the blood pressure method and the cat's uterus *in situ* method gave great individual variation in dogs and cats. Wood and Hofer (4) reported considerable variation in cats by the vasomotor reversal method. Broom and Clark (3) found considerable variation in some of the methods and concluded that the isolated guinea-pig uterus and the cat's uterus *in situ* measured the amine content of ergot, whereas, the cock's comb, vasomotor reversal action, and the isolated rabbit's uterus all measured the alkaloidal content of ergot, namely, ergotoxine and ergotamine. Broom and Clark further concluded that even though the rabbit's uterus and cock's comb are correlative in determining the alkaloidal content of ergot, the Cock's Comb Method shows greater variation than the Rabbit's Uterus Method, and suggested the later as the logical method for assaying ergot preparations.

More recently there have been a number of methods reported based on the epinephrine reversal action on the rabbit's uterus, Broom and Clark (3). Planelles

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* Scientific Section, A. PH A., Rapid City meeting, 1929.

[1] Department of Pharmacology, The Lilly Research Laboratories, Indianapolis, Indiana.

(5) used guinea-pig intestines; Masuda (6) tried the frog vessels and Raymond-Hamet (7) applied the renal vasomotors. Still more recently Nelson and Pattee (8) and Pattee and Nelson (9) have reported on the Isolated Rabbit's Uterus and also compared this method with the U. S. P. Cock's Comb Method. These authors found that the two methods yield results practically identical, that is, both methods determine the alkaloidal content of ergot. They also found that the U. S. P. Standard Fluidextract of Ergot by the Broom and Clark Method is approximately the equivalent of a 0.05 per cent solution of the specific alkaloids, which is about one-half the value of the standard set up by the Research Laboratory of the British Pharmaceutical Association as suitable for fluidextracts.

Considering the above review of the literature, it seems important to study the value of the Epinephrine Reversal Method (Broom and Clark) in the commercial assaying of ergot preparations and to compare this method with the Cock's Comb Method U. S. P.

Nelson and Pattee (8) and Pattee and Nelson (9) reported that there is considerable variation in potency of ergot preparations, particuarly, the solution of ergot for hypodermic use.

This article is the result of a comparative study of the Cock's Comb Method U. S. P. and the Broom and Clark Method, particularly of the latter, on a number of Fluidextracts of Ergot U. S. P. samples and solutions of ergot for hypodermic use, and also the hydrogen-ion concentration factor in relation to stability and deterioration.

2. METHODS OF ASSAY.

The Cock's Comb Method, U. S. P. is a well-known method and need not be described here. Gittinger and Munch (10) reported on this method and their results are in close agreement with our own findings.

The Rabbit's Uterus Method (Broom and Clark) involves the use of strings of uterine muscle in a constant temperature bath; the strips are immersed in Locke-Ringer's solution oxygenated by air and the muscles or strips arranged so as to record their contractions. Epinephrine reactions are first determined until these contractions are consistent to a certain degree, and then the ergot to be assayed is given to one muscle and the standard ergot to the other muscle. The ergot is allowed to remain in the cylinders five minutes, and then washed. The washing is important because Pattee and Nelson (9) has shown the antagonistic action of histamine. The amines, tyramine and acetylcholine, are now being studied and will be reported in another article. Following the washing or flushing of the muscle with fresh salt solution the same amount of epinephrine is injected or increased amounts of epinephrine are injected until the contractions are equal to the contractions of epinephrine before ergot paralysis. These factors will be described later.

3. SELECTION OF A MUSCLE.

The writer confirms the results of Burn (11) and Pattee and Nelson (9) in the use of large rabbits. The segregation of rabbits is helpful in obtaining suitable uteri. This also eliminates the influence of multiparous, post-partum and parturition factors. The segregation of young rabbits either virgin or monoparous, allowed to reach the weight of 3 or 4 Kg., is helpful in the choice of a suitable uterus.

The size of the individual uterus, regardless of the weight of the rabbit, is variable, but this is not so great when isolation is employed. Under these conditions of selection the uterine contractions are slow with little normal rhythm, resembling the guinea-pig uterus in the standardization of pituitary extract. A uterus with strong normal rhythmic contractions is usually too rapid in its contractions when stimulated with epinephrine and is not, in our findings, considered so reliable. Our experience favors the use of the whole uterus, that is, each fallopian tube is divided into two equal parts—thus supplying four strips. If the uterus is large, longitudinal cuts are made and divided into eight or more strips. Our findings favor the same degree of selection of a rabbit uterus as in the selection of guinea-pig uterus for pituitary testing. The writer prefers strips so cut as to give contractions of 40 mm. to 60 mm.

Much valuable time can be saved by external examination of the vaginal orifice as stated by Pattee and Nelson (9).

The selection of a choice uterus requires experience. It is the most difficult part of this method. For this reason the commercial application of this method in standardizing ergot preparations is still questionable.

4. TECHNIQUE OF ASSAYING.

Having selected a suitable uterus, the following three methods of technique have been studied:

A. *Complete paralysis* of the uterus by ergot.
B. *Partial paralysis* of uterus.
C. *The ratio of epinephrine stimulation to ergot paralysis.*

Method A.—The application of large doses of ergot to cause complete paralysis or inhibition to epinephrine stimulation is not consistent for all uterine muscle, that is, some uteri require more or less ergot to produce inhibition. It is possible, however, by this technique to assay an ergot preparation by determining on a number of muscles the minimum amount of ergot in comparison to a standard ergot as a control that will cause inhibition or paralysis. (See Fig. 1, the lower tracing.)

Method B.—Partial paralysis involves the use of small doses of ergot (both standard and unknown) that will only partially inhibit the epinephrine stimulation. Gradually decreasing doses of epinephrine are injected, until quantitative contractions are obtained and then a small dose of ergot is injected, five minutes duration allowed, washed once or twice and finally the same amount of epinephrine is injected as before ergot application. The amount of inhibition is measured, compared with the control and the amount of reduction in contraction calculated. Injections of epinephrine are repeated until the contractions of the uterus return to constant height with the same amount of epinephrine. When the contractions are constant ergot is again injected and the same technique repeated as above. Thus small doses of ergot or partial paralysis permits the injection of several doses of ergot on the same uterus, and by alternating the unknown and standard on the same muscle one can obtain fairly accurate comparisons, see Figs. 1, 2, 3 and 4.

Method C.—This technique determines the amount of paralysis in terms of epinephrine, that is, following the ergot paralysis the amount of epinephrine in-

jected is increased until the contraction equals in height the contraction of epinephrine before ergot was injected. Thus the amount of increase in epinephrine depends upon the amount of ergot injected or the degree of paralysis caused by ergot. As in Figs. 2 and 3, 1 cc. (1–100) Fluidextract of Ergot U. S. P. produced a 1 to 2 ratio in epinephrine and 0.005 mg. of ergotoxine produced a 1 to $2^2/_3$ ratio. Therefore this Fluidextract of Ergot U. S. P. contained 0.0375% of alkaloid in terms of ergotoxine phosphate.

All of the above three methods give fairly accurate results. Methods B and C are more reliable in that the same muscle may be used for the standard and the unknown. Method C, theoretically, seems to be the most reliable because ergot paralysis is balanced against epinephrine stimulation. The assays in the following tables are based on Methods A and B. Method C is being more extensively studied and will be reported in a later article.

5. EXPERIMENTAL DATA.

The following data represents a number of Fluidextracts of Ergot U. S. P. These samples are manufactured lots, each being assayed by the Cock's Comb and Reversal Uteri (Broom and Clark) Methods.

TABLE I.

Data.	F. E. Ergot, U. S. P., sample no.	Cock's Comb Method, per cent activity.	Reversal Uteri, Broom and Clark. Alkaloidal content.	Reversal Uteri, Broom and Clark. Per cent activity.
6– 2–27	1	100%	0.050%	100%
8–31–27	2	100%	0.050%	100%
11– 1–27	3	90%	0.045%	90%
10–23–28	4	100%	0.050%	100%
11–10–28	5	80%	0.045%	90%
7–30–28	6	100%	0.055%	110%

These results show that the two methods correlate in determining the alkaloidal content of fluidextracts.

One-half gallon of fluidextract of ergot was reserved from a manufactured lot and divided into eight equal parts. One of the samples or parts contained no acid, to the remaining seven parts various amounts of HCl 36% were added so as to have various hydrogen-ion concentrations. The original assays by the Cock's Comb and Reversal Uteri (Broom and Clark) Methods were 90% and 100%, respectively.

The following table shows the assays of these samples after two years' aging.

TABLE II.

F. E. Ergot, sample no.	P_H.	Cock's Comb Method, per cent activity.	Broom and Clark Method. Alkaloidal content.	Broom and Clark Method. Per cent activity.
1	5.35	less 10%	0.001%	2%
2	4.95	16%	0.002%	4%
3	4.51	40%	0.02%	40%
4	3.77	60%	0.03%	60%
5	3.21	80%	0.04%	80%
6	2.69	80% to 90%	0.05%	100%
7	2.26	..	0.05%	100%
8	1.90	90%	0.05%	100%

Inspection of the above table shows that by both methods the results are correlative. The two methods determine the alkaloidal content of ergot. The cock's comb assay is less reliable as the deterioration increases. This may be due to the large amount of ergot that is required to be injected into the breast muscle of the cock.

The hydrogen-ion concentration factor shows that the Fluidextract of Ergot requires a certain amount of acid to prevent deterioration. Sample No. 5 contained the same amount of acid that is required by the U. S. P. A p_H value of 3.00 is necessary to prevent deterioration. See Chart I.

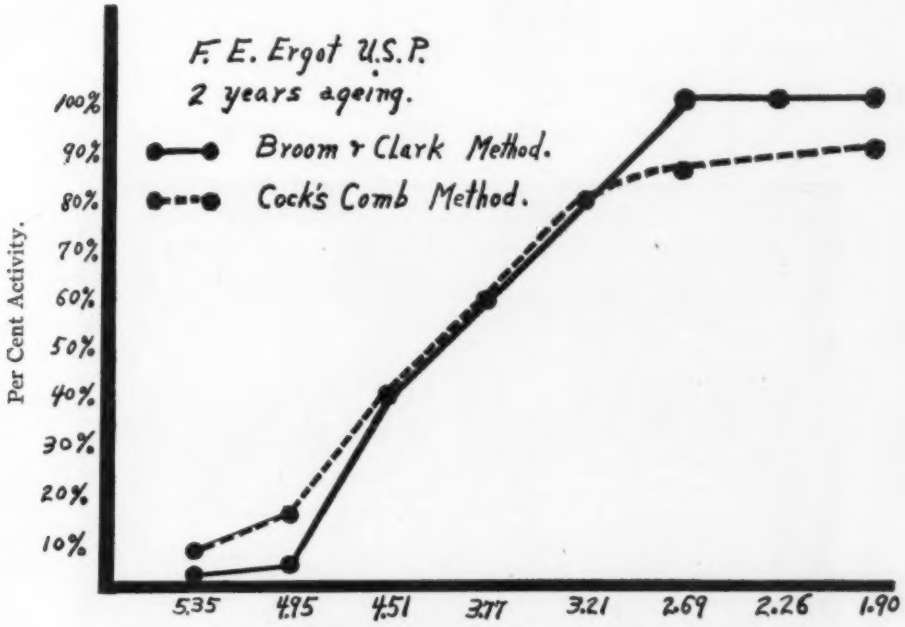

Chart I.—Hydrogen-ion concentration.

A number of solutions of ergot for hypodermic use were assayed by the two methods. The results are as follows:

TABLE III.

Solution no.	Date made.	Date assayed.	Cock's Comb Method.	Broom and Clark. Alkaloidal content.	Broom and Clark. Per cent activity.
1	9–29–26	2–27–28	50% to 60%	0.010%	20%
2	1–14–27	2–27–28	125%	0.040%	80%
3	10–29–27	2–27–28	125%	0.080%	160%
4	11– 2–27	3– 6–28	140%	0.080%	160%

These solutions were made so that 1 cc. contained the equivalent of 2 Gm. of ergot drug. The original assay of the four samples was 200% by the Cock's Comb Method. No assay was made by the Broom and Clark Method. There is no question from inspection of the above table, that solutions of ergot for hypodermic use deteriorate rapidly. This is in agreement with that reported by Pattee and Nelson (9). This deterioration may be a hydrogen-ion concentration factor.

In order to determine the question of the hydrogen-ion concentration a solution of ergot for hypodermic use was prepared August 1928, 1 cc. contained the equivalent of 2 Gm. of drug and assayed 150% by the Cock's Comb method. This solution was divided into six parts; each sample or part was treated with 36% HCl so as to have various hydrogen-ion concentrations. These samples are now being assayed by the two methods to determine stability following a year's aging.

TABLE IV.

Sample no.	P_H.	Date.	Cock's Comb Method, %.	Broom and Clark Method. Alkaloidal content.	Broom and Clark Method. Per cent activity.
1	4.30	8-20-28	150%	0.08%	160%
2	3.20	8-20-28	...	....	...
3	2.90	8-20-28	...	....	...
4	2.40	8-20-28	...	....	...
5	1.90	8-20-28	...	....	...
6	1.75	8-20-28	150%	0.08%	160%

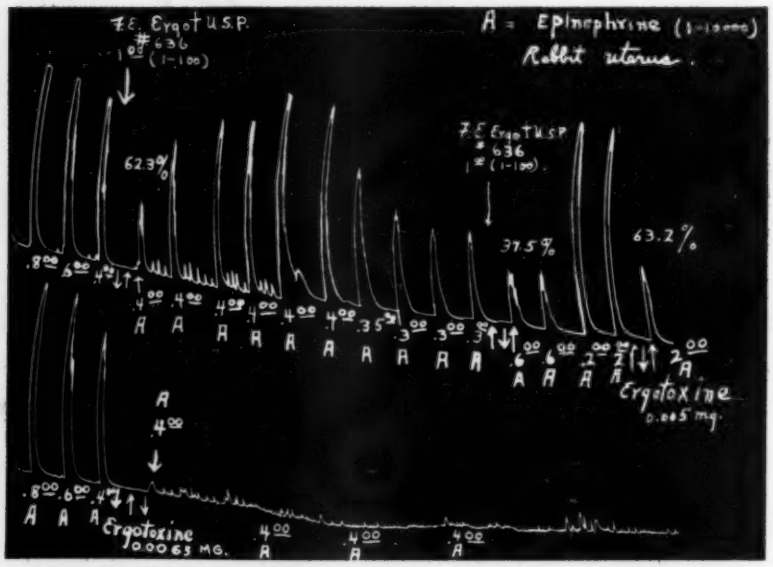

Fig. 1.—The upper tracing represents Methods B and C. The lower tracing represents Method A.

The results of the above assays following one year's aging will be reported later.

6. ERGOTOXINE AND ERGOTAMINE RELATIONSHIP.

In regard to the alkaloids of ergot, ergotoxine and ergotamine, the writer is in agreement with Pattee and Nelson that ergotoxine is distinctly more active than ergotamine. The average figures of more than a hundred tests show the following equivalents: 1 mg. Ergotoxine base is the equivalent of 1.3 mg. Ergotamine base. In Figs. 1, 2, 3 and 4 the Fluidextract of Ergot U. S. P. No. 636 is a standard preparation obtained from the Pharmacological Laboratory of the Bureau of Chemistry of the United States Department of Agriculture. This fluidextract

contains 0.050% of alkaloid in terms of ergotoxine phosphate or 0.0422% of ergotoxine base or 0.0522% of ergotamine base (1 mg. ergotoxine base = 1.3 mg.

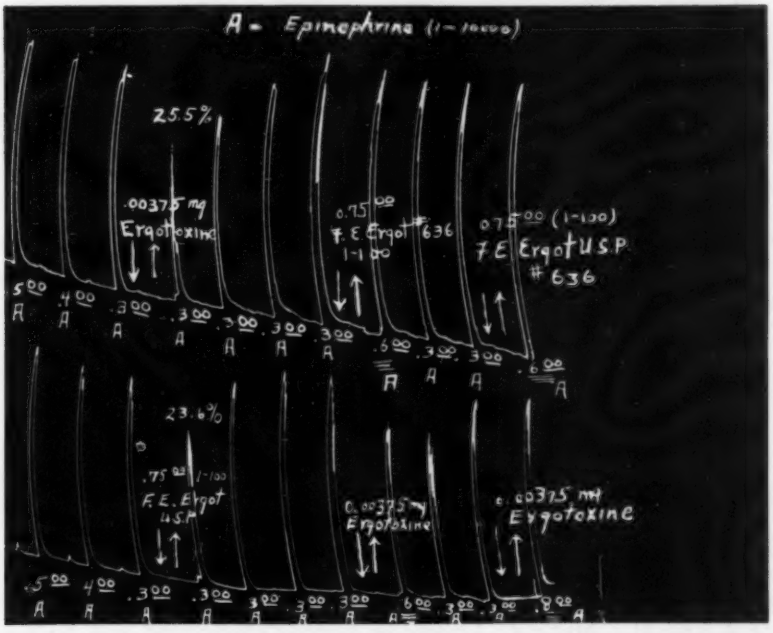

Fig. 2.—This tracing illustrates Methods B and C.

ergotamine base) as assayed by the above Methods A and B. However, by Method C the same Fluidextract of Ergot U. S. P. No. 636 assays 0.0375% of alkaloid in

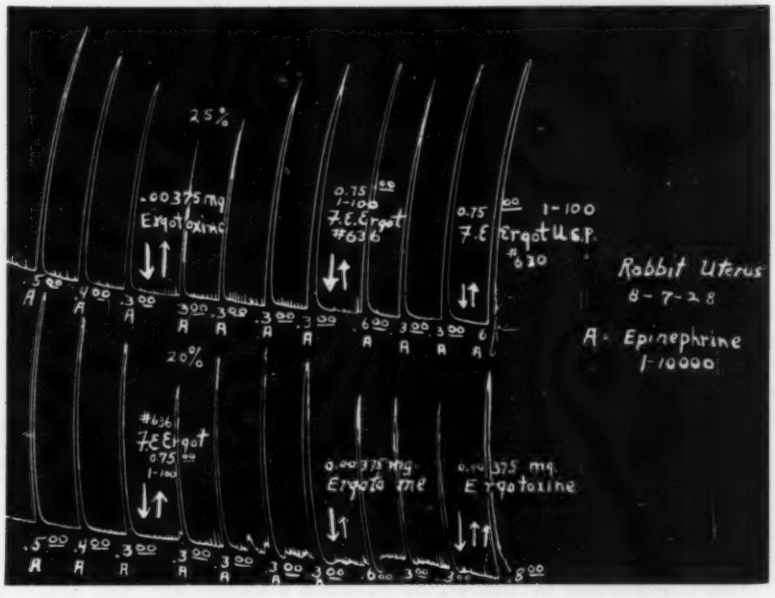

Fig. 3.—This tracing illustrates Methods B and C.

terms of ergotoxine phosphate, or 0.0316% in terms of ergotoxine base or 0.0410% of ergotamine base.

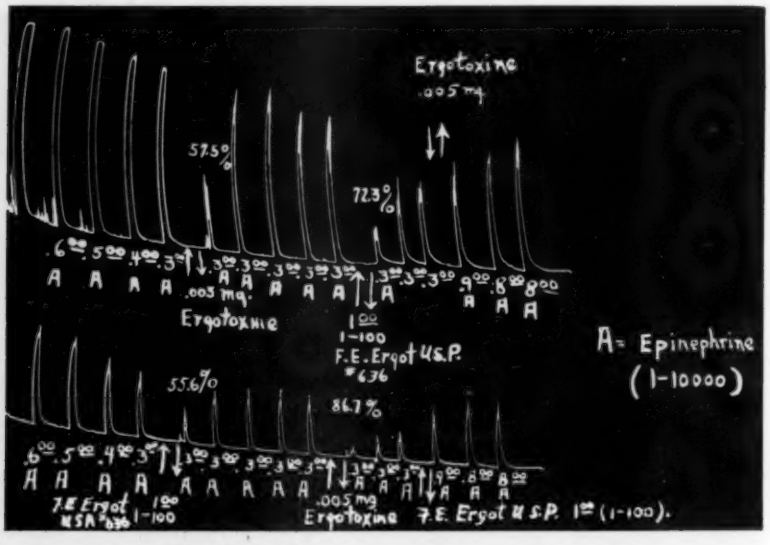

Fig. 4.—This tracing illustrates Methods B and C.

As stated previously the tests in the Tables I, II, III and IV were made by Methods A and B. Method C requires further study and will be reported in another article.

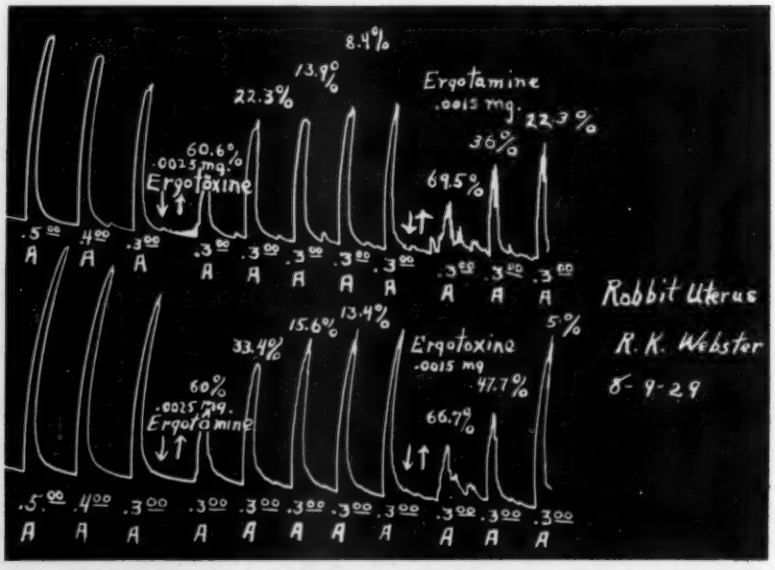

Fig. 5.—This tracing illustrates Method B.

7. SUMMARY.

1. The comparison of the U. S. P. Cock's Comb Method and the Broom and Clark Method gave similar results on a number of fluidextracts and solutions

or ergot. The Broom and Clark Method involves more skill and technique than the U. S. P. X. Some modifications of the Broom and Clark Method are being studied and further work is in progress.

2. The F. E. Ergot U. S. P. seems to be comparatively stabile, although further tests are necessary.

3. The solution of ergot for hypodermic use deteriorates rapidly.

4. A Fluidextract of Ergot was treated with various amounts of acid. The hydrogen-ion concentration seems to have some influence in controlling the deterioration and stabilization.

5. Further experiments are now in process to determine the value of the hydrogen-ion concentration factor.

6. Ergotoxine is distinctly stronger than ergotamine. The writer is much indebted to Dr. H. W. Cole for criticism of manuscript, to F. A. Whipple for hydrogen-ion concentration determinations, and to R. K. Webster, C. E. Powell and C. C. Hargreaves for assistance in making some of the tests.

EXPLANATION OF ILLUSTRATIONS.

Figure 1 represents a rabbit uterus (one fallopian tube cut in two equal parts). Gradually decreasing doses of epinephrine were injected, then to the upper muscle 1 cc. of 1–100 dilution of F. E. Ergot U. S. P. No. 636 was injected into the 100 cc. chamber, the ergot allowed to remain in contact with the muscle 5 minutes, then washed and the same amount of epinephrine is added as before ergot injection. The paralysis of ergot caused a 62.3% reduction or inhibition. The same muscle was given repeated injections of epinephrine. Note the recovery of the muscle to epinephrine stimulation. Two injections of 3 cc. (1–10,000) of epinephrine produced equal contractions. 1 cc. (1–100) F. E. Ergot U. S. P. No. 636 was again injected, 5 minutes' duration allowed, washed and 0.6 cc. of epinephrine added. This produced only 37.5% inhibition or reduction. Two cc. of 1–10,000 epinephrine was injected twice, 0.005 mg. of ergotoxine injected, which produced a 63.2% reduction or inhibition. The lower muscle received gradually decreasing amounts of epinephrine, then 0.0065 mg. of ergotoxine was added. This produced complete inhibition or paralysis to further 0.4 cc. (1–10,000) doses of epinephrine. Therefore, F. E. Ergot U. S. P. No. 636 contains 0.005 mg. of ergotoxine phosphate per 1 cc. (1–100) or 0.05% of ergotoxine phosphate according to the upper tracing or muscle.

Figure 2 represents a rabbit uterus (one fallopian tube cut in two equal parts). Gradually decreasing doses of epinephrine were injected, then to the upper muscle 0.00375 mg. of ergotoxine and the lower muscle 0.75 cc. 1–100 F. E. Ergot U. S. P. No. 636 were injected, 5 minutes' duration allowed, and washed. This produced a reduction of 25.5% with ergotoxine to the upper muscle. The lower tracing or muscle shows a 23.6% reduction or inhibition with the F. E. Ergot U. S. P. No. 636. Compare this with Fig. 1, which received 1 cc. (1–100) of F. E. Ergot U. S. P. No. 636 and 0.005 mg. of ergotoxine and gave 62.3% and 63.2% paralysis, respectively.

Repeated injections of epinephrine shows a gradually returning response. Following three injections of epinephrine 0.75 cc. (1–100) F. E. Ergot U. S. P. No. 636 and 0.00375 mg. of ergotoxine were injected, then washed after 5 minutes' duration, and then 0.6 cc. (1–10,000) of epinephrine or twice the dose of epinephrine as before ergot was injected. The upper tracing shows equal contractions, the lower tracing did not come up to the control—thus assuming that 0.00375 mg. of ergotoxine is stronger than 0.75 cc. 1–100 of F. E. Ergot. Later the same doses were given but to the lower muscle 0.8 cc. of epinephrine was injected which equaled the previous contraction. According to this tracing the F. E. Ergot U. S. P. No. 636 contains slightly less than 0.05% of ergotoxine phosphate.

Figure 3 represents the same rabbit uterus as Fig. 2, but is the other fallopian tube cut into two equal parts. The same treatment was applied to these muscles as in Fig. 2. Note the similarity of action as in Fig. 2. The lower tracing is not so reliable because the pointer seemed to scratch and the operator could not make adjustments without causing irregularities.

Figure 4 represents a rabbit uterus. Gradually decreasing doses of epinephrine were injected, which show a gradual decrease in contractions. To the upper muscle 0.005 mg. of ergotoxine and to the lower muscle 1 cc. 1–100 F. E. Ergot U. S. P. No. 636 were injected. This produced a reduction or inhibition of 57.5% and 55.6%, respectively. The same injections were later repeated only reversed (the upper receiving ergotoxine and the lower F. E. Ergot). This gave a reduction or inhibition of 72.3% and 86.7%, respectively. This tracing shows that 0.005 mg. of ergotoxine is slightly stronger than 1 cc. 1–100 F. E. Ergot U. S. P. No. 636.

Figure 5 represents a rabbit uterus (one fallopian tube cut into equal parts); 0.0025 mg. of ergotoxine and 0.0025 mg. of ergotamine produced inhibition or partial paralysis, 60.6% and 60%, respectively. Repeated equal-size doses of epinephrine show a gradual recovery, each succeeding repeating dose showing a decrease in inhibition or reduction. For ergotoxine 60.6%, 22.3%, 13.9% and 8.4% and finally back to the control.

For ergotamine 60%, 33.4%, 15.6%, 13.4% and finally almost to the control.

A second injection of these drugs with smaller doses of 0.0015 mg., but reversed, show a reduction or inhibition of 69.5%, 36% and 22.3% for ergotamine and 66.7%, 47.7% and 5% for ergotoxine. This tracing seems to show that ergotoxine is about equal to ergotamine, however, many tests similar to this show that ergotoxine is distinctly stronger than ergotamine.

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(9) Pattee and Nelson, *J. Pharmacol. & Exper. Therap.*, 36 (1929), 85.
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(11) J. H. Burn, *Pharm. J.*, 117 (1926), 576.

ABSTRACT OF DISCUSSION.

M. R. Thompson, commenting on the results of the experiments, said that the amines or water-soluble substances could occur in certain substances and might interfere greatly in the Cock's Comb or other methods.

E. E. Swanson stated that Pattee and Nelson, *J. Pharmacol. & Exper. Therap.*, 36 (1929), found that histamine inhibited the action of ergotamine. Also Dr. A. J. Clark, co-author of the Broom and Clark Method, observed that washing is necessary in order to prevent the antagonistic action of the amines. This has also been verified by the experiments of the authors, who found that two or three washings are sometimes necessary to abolish the amine antagonistic action.

M. R. Thompson further commented that certain investigators in this country have used this Broom and Clark Method and modified it in such a manner as to avoid washing after the administration of the ergot preparation, and then followed by the epinephrine. This technic cannot be used in preparations which are high in amines, and which greatly interfere with the activity. The effect will be one of low potency because the amines have a tendency to sensitize the uterus and the alkaloids will diminish the effect.

In regard to samples of ergotoxine, the results in their activity have been variable, whereas ergotamine samples do not vary.

James C. Munch remarked that Dr. A. J. Clark, in a personal interview, said that he found washing was necessary with uteri from certain breeds of rabbits.

E. F. Cook stated that it might be permissible to mention a new method just being proposed, an assay which gives some promise—that of Reynold and Carlson, which will be published in the *Journal of Physiology* in October. They use the living rabbit, determining the effect of the pituitary and also ergot on the uterus. They operate and draw out the uterus through the side of the rabbit, establishing a fistula. When the experiment is complete they make direct

observations of the contractions of the uterus. They discovered there was a certain period, possibly seven days during each month, when the uterus would not react, and so they were compelled to utilize the period when the uterus was responsive. They secured very definite readings from the contraction of the uterus.

F. O. Taylor requested information as to what acid was used for developing the p_H value of different samples tested for stability, and also if these samples were assayed chemically.

Mr. Swanson stated that no chemical test was tried.

ABSTRACTS OF PAPERS OF SCIENTIFIC SECTION, A. PH. A., 1929.

"Coal Tar Food Colors," by S. E. Owen.

Colors obtained in dying wool from acid and alkaline solutions recorded. Some general chemical tests are also given for differentiation of various colors.

"Amino Alcohols: 4. Reactions with Alkaloidal Reagents," by James C. Munch and W. H. Hartung.

Precipitation and color reactions of series of products homologous with ephedrine are reported.

"Amino Alcohols: 5. A Potentiometric Study of Certain Homologues of Ephedrine," by John C. Krantz, Jr., and W. H. Hartung.

A potentiometric study including the degrees of hydrolysis and association constants of certain homologs of ephedrine is reported.

"Ultraviolet Transmission of Liquids," by Ellery H. Harvey.

Transmission ultraviolet light measured by decomposition oxalic acid catalyzed by uranium salts. Tested large group of essential, fatty and crude oils as well as liquid chemicals. Application to storage in various wave-lengths of light discussed.

"Olive Oil—Fluorescence in Ultraviolet Light," by L. Deuble and R. E. Schoetzow.

The value of ultraviolet light as a means of detecting the presence of refined or treated olive oil in virgin olive oil is discussed.

"A Comparison of the Tissue Toxicity and Germicidal Power of Germicides," by Lester C. Himebaugh and Emil C. Fanto.

The toxicity of various germicides to living tissues grown outside the body has been compared with their germicidal action.

"Comments on U. S. P. X test for Rhapontic Rhubarb," by R. A. Konnerth and R. E. Schoetzow.

The unreliability of the U. S. P. test is pointed out and the more reliable method of the German Pharmacopœia is recommended.

"Digitalis Investigations. III. Digitalis Seed, Histology and Microchemistry," by Arno Viehoever and K. Shinohara.

Morphological, histological characteristics have been established. The presence and distribution of the active constituents was ascertained by microchemical methods. Digitalin and Digitonin are present in the endosperm and embryo. Digitalin occurs in larger amounts in the mature than in the immature seed.

"Pharmacognosy of Psyllium Seed," by Arno Viehoever and E. L. McLaughlin.

Morphological characteristics as well as histological have been established. A new method for the quantitative determination of the water-soluble mucilage in the outer seed coat has been devised. About 2.5 per cent of ash-free mucilage has been found in commercial seed as well as that grown under controlled conditions.

"Reactions between Formaldehyde and Hydrogen Peroxide and Quantitative Method Based Thereupon," by Arno Viehoever and K. Shinohara.

The various chemical reactions between Formaldehyde and Hydrogen Peroxide have been studied and a quantitative method of determination evolved.

"Digitalis Investigations. I. Effect of Digitoxin on the Heart of Daphnia Magna," by Arno Viehoever and A. McReyya.

Saturated aqueous solution increased tone of heart muscle and heart stopped in five to six hours. Toxic effect observed sooner in the presence of chloroform.

"Digitalis Investigations. II. Effect of Digitonin on the Heart of Daphnia," by Arno Viehoever and Manuel Tubis.

Saturated aqueous solution of digitonin behaved in general like saponin solution. A general slowing of the heart beat was observed, also slowing of antennae and increased peristalsis.

DIGITALIS ASSAY STANDARDS.*

BY L. W. ROWE.[1]

In spite of the wide-spread consideration which the bio-assay of digitalis and other members of this group of heart tonics has received in recent years as evidenced by the many published articles proposing slightly modified methods, the standards suggested for the different methods have seldom been compared. When one says that a certain Tincture of Digitalis has been standardized by the Houghton M. L. D. Frog-Heart Method to contain 6.6 Heart Tonic Units and is therefore of 100% activity, what relation has such a tincture to one which is 100% by the Cat Method?

It is the purpose of this short paper to present data giving average experiences over a period of years with comparative tests of representative samples by several of the more frequently used methods so as to give some basis for comparison between products standardized by different methods.

The methods chiefly concerned will be the M. L. D. Frog-Heart (Houghton), the One-Hour (Official, U. S. P.), the Cat (Hatcher), with occasional tests by the Four-Hour Frog (Geneva Conference) and the M. L. D. Guinea-Pig (Reed and Vanderkleed). The details of the technique of these methods will not be given here as they are easily available in other published articles and scarcely need repetition. The test data will be tabulated so as to compare results by each method with those by the Official One-Hour Frog Method. A few tests of Digitalin and Strophanthin are also included.

From the data in Tables I and II and the summarized percentages and ratios in Table III, it is seen that the four main standards for Tincture of Digitalis, namely (1) U. S. P. One-Hour Frog Method standard (1 cc. Tincture = 0.083 mg. U. S. P. Ouabain), (2) the M. L. D. Frog-Heart Method (Houghton) standard (1 cc. Tincture = 0.033 mg. U. S. P. Ouabain), (3) the Cat Method (Hatcher) standard (1 cc. Tincture = 0.1 mg. U. S. P. Ouabain), (4) the Four-Hour Frog Method (International) standard, (1 cc. Tincture = 1 cc. Tincture from standard leaf), are actually not very different as judged by the average results on a number of samples each tested by more than one method.

Roughly it seems that the One-Hour Method (U. S. P.) standard may be about 10% *more* active than the M. L. D. Frog Method standard and about 10% *less* active than the Cat Method standard thus making the latter about 20% higher than the standard of the M. L. D. Frog Method. As for the Four-Hour Frog Method (International) standard, this seems to be about equal to the One-Hour Method standard and consequently 10% more active than the M. L. D. Frog Method standard and 10% less active than the Cat Method standard. The Guinea-Pig Method standard is apparently about right, that is, equal to the One-Hour Method standard but an insufficient number of tests on Tincture of Digitalis, one of which was on a sample where the One-Hour Method result was apparently low, made the ratio seem to be in favor of the One-Hour Standard.

As for the actual standards, I do not favor Ouabain as the standard for Digitalis since its action on the various animals in the more frequently used methods

* Scientific Section, A. PH. A., Rapid City meeting, 1929.

[1] Research Laboratories of Parke, Davis & Co., Detroit, Michigan.

is much more rapid due to better absorption and a naturally faster toxic action on the heart. It is a suitable standard for Strophanthus activity, however. The international standard Digitalis leaf used as a freshly prepared tincture is no doubt the best standard which is available at present for Digitalis assay. The potency of this international standard Digitalis leaf is apparently about equal to the standard set in the present U. S. P. and consequently is a practical and easily attainable standard which will not place too potent a tincture of digitalis in the hands of the average physician. Thus the equivalent of the present international standard Digitalis leaf would seem from many considerations to be a better standard for the next U. S. P. than is our present Ouabain standard.

The Cat Method standard is apparently the most active of all the standards proposed for Tincture of Digitalis and the method itself is open to criticism from the standpoint of accuracy since in eliminating the absorption factor, it frequently fails to show deterioration in tinctures which have been shown both clinically and by other bio-assay methods to have lost potency very definitely.

While a consideration of the choice of a method of digitalis assay is a little beyond the scope of this paper, it seems logical to go on record on the basis of years of experience with the better known methods as being definitely opposed to the present One-Hour Method because of the indefiniteness of its end-point under actual conditions due to too short a period of absorption of a slowly acting drug, and to favor an M. L. D. method in which a long enough period of time is allowed to elapse for the complete absorption and toxic action of the dose injected. The Four-Hour Frog Method proposed by the International Conference is entirely satisfactory for the assay of Strophanthus preparations where the action of the drug is more rapid, but for Digitalis the four-hour period is scarcely long enough for complete absorption and action even at 20° C.; for Digitalis the time limit should be placed at six hours at least for definite and easily comparable results.

CONCLUSIONS.

1. Comparisons of the various standards proposed in the more important methods for the assay of Tincture of Digitalis, by means of tests of a number of samples, each by more than one method, show that the standard set for the Cat Method is fully 10% higher than that set for the One-Hour Method and the Four-Hour Frog Method (these two seem about equal) while the standard originally set 30 years ago for the M. L. D. Frog Method is not more than 10% lower than the present U. S. P. standard.

2. Very few comparative results were obtained with the guinea-pig method but the data pointed to the standard suggested being about right, that is, equal to that of the One-Hour and Four-Hour Methods for both Tr. Digitalis and Ouabain.

3. The present U. S. P. standard for Tincture of Digitalis, namely, Ouabain, is not satisfactory and it is suggested that the international standard Digitalis leaf or its equivalent be adopted as the standard for Tincture of Digitalis in the next U. S. Pharmacopœia.

4. The official method for the assay of Digitalis preparations (the One-Hour Frog Method) as recommended in the present U. S. P. is not satisfactory and it is suggested that an M. L. D. Method with a time limit of at least six hours be considered for recommendation in the next U. S. Pharmacopœia.

TABLE I.

Sample.	One-Hour M. S. D. (per Gm.).	In terms of U. S. P. Ouab.	Frog Heart M. L. D. (per Gm.).	In terms of U. S. P. Ouab.	Cat intrav. M. L. D. per Kg.	In terms of U. S. P. Ouab.
Tr. Digitalis A, 1	0.010 cc.	1 cc. = 0.070 mg.	0.012 cc.	1 cc. = 0.030 mg.		
Tr. Digitalis A, 2	0.011 cc.	1 cc. = 0.064 mg.	0.010 cc.	1 cc. = 0.036 mg.	1.14 cc.	1 cc. = 0.088 mg.
Tr. Digitalis A, 3	0.011 cc.	1 cc. = 0.064 mg.	0.011 cc.	1 cc. = 0.033 mg.		
Tr. Digitalis B, 1	0.009 to 0.010 cc.	1 cc. = 0.074 mg.	0.012 cc.	1 cc. = 0.030 mg.		
Tr. Digitalis B, 2	0.010 cc.	1 cc. = 0.070 mg.	0.012 cc.	1 cc. = 0.030 mg.	1.42 cc.	1 cc. = 0.070 mg.
Tr. Digitalis B, 3	0.009 cc.	1 cc. = 0.078 mg.	0.010 cc.	1 cc. = 0.036 mg.		
Tr. Digitalis No. 1–22	0.008 cc.	1 cc. = 0.075 mg.	0.014 cc.	1 cc. = 0.021 mg.	1.80 cc.	1 cc. = 0.055 mg.
Tr. Digitalis No. 2–22	0.012 cc.	1 cc. = 0.050 mg.	0.016 cc.	1 cc. = 0.019 mg.	1.95 cc.	1 cc. = 0.051 mg.
Tr. Digitalis No. 3–22	0.014 cc.	1 cc. = 0.043 mg.	0.022 cc.	1 cc. = 0.014 mg.	2.36 cc.	1 cc. = 0.042 mg.
Tr. Digitalis S-22	0.006 cc.	1 cc. = 0.080 mg.	0.005 cc.	1 cc. = 0.060 mg.	0.86 cc.	1 cc. = 0.116 mg.
Digitalin No. 309390	0.00025 Gm.	1 Gm. = 3.3 mg.	0.00012 Gm.	1 Gm. = 2.5 mg.	6.23 mg.	1 Gm. = 16 mg.
Ouabain U. S. P., 1927	0.0000008 Gm.		0.00000033 Gm.		0.097 mg.	
Ouabain U. S. P., A. D. M. A.	0.0000006 Gm.		0.00000036 Gm.		0.105 mg.	
Ouabain U. S. P., 1928	0.0000005 Gm.		0.0000003 Gm.			
Digitalin A. D. M. A.	0.00010 Gm.	1 Gm. = 6 mg.	0.00011 Gm.	1 Gm. = 2.45 mg.	6.15 mg.	1 Gm. = 16 mg.
Digitalin D. C. C.	0.00020 Gm.	1 Gm. = 3 mg.	0.00014 Gm.	1 Gm. = 2.2 mg.	10 mg.	1 Gm. = 10 mg.
Tr. Digitalis No. 2791741			0.022 cc.	1 cc. = 0.016 mg.	1.46 cc.	1 cc. = 0.068 mg.
Tr. Digitalis Intern't'l St'd	0.008 cc.	1 cc. = 0.083 mg.	0.006 cc.	1 cc. = 0.045 mg.	1.05 cc.	1 cc. = 0.095 mg.
Tr. Digitalis "S"	0.005 cc.	1 cc. = 0.10 mg.	0.006 cc.	1 cc. = 0.050 mg.	0.76 cc.	1 cc. = 0.132 mg.
Tr. Digitalis A	0.012 cc.	1 cc. = 0.05 mg.	0.010 cc.	1 cc. = 0.030 mg.		
Tr. Digitalis B	0.009 cc.	1 cc. = 0.067 mg.	0.0085 cc.	1 cc. = 0.038 mg.		
Tr. Digitalis C	0.010 cc.	1 cc. = 0.060 mg.	0.014 cc.	1 cc. = 0.023 mg.		
Strophanthin Kombé	0.0000005 Gm.	1 Gm. = 1 Gm.	0.00000055 Gm.	1 Gm. = 0.55 Gm.		
Digitalin No. 295460	0.00006 Gm.	1 Gm. = 10 mg.	0.00006 Gm.	1 Gm. = 6 mg.		
Digitalin No. 49929	0.00015 Gm.	1 Gm. = 4 mg.	0.00012 Gm.	1 Gm. = 3 mg.		

TABLE II.

Sample.	One-Hour Frog M. S. D.	In terms of U. S. P. Ouab.	Four-Hour Frog M. L. D.	In terms of U. S. P. Ouab.	Guinea-pig M. L. D.	In terms of U. S. P. Ouab.
Ouabain U. S. P.	0.0000006 Gm.		0.0000003 Gm.		0.0000002 Gm.	
Tr. Digitalis Intern't'l St'd	0.008 cc.	1 cc. = 0.075 mg.	0.005 cc.	1 cc. = 0.05 mg.	0.003 cc.	1 cc. = 0.067 mg.
Tr. Digitalis S-22	0.006 cc.	1 cc. = 0.08 mg.			0.0015 cc.	1 cc. = 0.13 mg.
Tr. Digitalis No. 2465655			0.015 cc.	1 cc. = 0.027 mg.	0.006 cc.	1 cc. = 0.033 mg.
Strophanthin Kombé	0.0000005 Gm.	1 Gm. = 1 Gm.	0.00000055 Gm.	1 Gm. = 0.55 Gm.		
Digitalin A. D. M. A.	0.00010 Gm.	1 Gm. = 6 mg.	0.00015 Gm.	1 Gm. = 2.0 mg.	0.000035 Gm.	1 Gm. = 5.7 mg.
Digitalin No. 295460	0.00006 Gm.	1 Gm. = 10 mg.			0.000015 Gm.	1 Gm. = 13 mg.
Digitalin No. 49929	0.00015 Gm.	1 Gm. = 4 mg.			0.000025 Gm.	1 Gm. = 8 mg.
Digitalin DCC	0.00020 Gm.	1 Gm. = 3 mg.			0.000040 Gm.	1 Gm. = 5 mg.

TABLE III.

Sample.	% of std.* One-Hour Method, per cent.	% of std.* M. L. D. Frog Method, per cent.	% of std.* Cat Method. per cent.	% of std.* Guinea-Pig M. L. D., per cent.	% of std. Four-Hour Frog, per cent.	Ratios.
Tr. Digitalis A, 1	84	90				1 to 1.07
Tr. Digitalis A, 2	77	108	88			1 to 1.40 to 1.14
Tr. Digitalis A, 3	77	100				1 to 1.30
Tr. Digitalis B, 1	89	90				1 to 1.01
Tr. Digitalis B, 2	84	90	70			1 to 1.07 to 0.83
Tr. Digitalis B, 3	94	108				1 to 1.14
Tr. Digitalis 1–22	90	63	55			1 to 0.70 to 0.61
Tr. Digitalis 2–22	60	56	51			1 to 0.93 to 0.85
Tr. Digitalis 3–22	52	42	42			1 to 0.81 to 0.80
Tr. Digitalis S–22	96	180	116	165		1 to 1.87 to 1.2 to 1.72
Tr. Digitalis No. 2791741		48	68			0 to 1 to 1.40
Tr. Digitalis Inter. Std.	100	135	95	83	100	1 to 1.35 to 0.95 to 0.83 to 1
Tr. Digitalis Spec.	120	150	132			1 to 1.25 to 1.1
Tr. Digitalis A	60	90				1 to 1.50
Tr. Digitalis B	80	112				1 to 1.40
Tr. Digitalis C	72	68				1 to 0.94
Tr. Digitalis No. 2465655		72		42	54	0 to 1 to 0 to 0.58 to 0.75
Ouabain U. S. P.	100	90	97	100	100	1 to 0.9 to 0.97 to 1 to 1
Strophanthin Kombé	200	100			110	1 to 0.50 to 0 to 0 to 0.55
Digitalin A. D. M. A.	No std.	45	58	46	No std.	0 to 1 to 1.30 to 1.02
Digitalin No. 309390	No std.	45	58			0 to 1 to 1.30
Digitalin D. C. C.	No std.	36	36	40		0 to 1 to 1 to 1.1
Digitalin No. 295460	No std.	112		100		0 to 1 to 0 to 0.9
Digitalin No. 49929	No std.	56		64		0 to 1 to 0 to 1.14

Footnotes referred to by asterisks—One-Hour standard, 1 cc. Tincture of Digitalis = 0.083 mg. U. S. P. Ouabain. M. L. D. Frog standard, 1 cc. Tincture of Digitalis = 0.033 mg. U. S. P. Ouabain.

Cat Method standard, 1 cc. Tincture of Digitalis = 0.1 mg. U. S. P. Ouabain. Guinea-Pig Method standard, 1 cc. Digitalis = 0.08 mg. U. S. P. Ouabain.

Average ratio One-Hour Method standard to M. L. D. Frog Method standard is 1 to 1.12.

Average ratio One-Hour Method standard to Cat Method (Hatcher) standard is 1 to 0.94.

Average ratio One-Hour Method standard to Guinea-Pig Method standard is 1 to 1.18 (3 comp.).

Average ratio One-Hour Method standard to Four-Hour Method standard is 1 to 1.0 (2 comp.).

Average ratio M. L. D. Frog Method standard to Cat Method standard is 1 to 0.83 (8 comp.), Cat standard is 20% higher.

Average ratio M. L. D. Frog Method standard to Guinea-Pig standard is 1 to 0.92 (8 comp.), Guinea-Pig standard is 10% higher.

Average ratio M. L. D. Frog Method standard to Four-Hour Frog standard is 1 to 0.70 (2 comp.).

ABSTRACT OF DISCUSSION.

E. E. Swanson stated that an interesting study of methods and standards had been presented, and indicates that the methods should be studied with the view of harmonizing or selecting a method for adoption. He thought that the Hanzlik Pigeon Emesis Method was deserving of consideration because of the amount of work that had been done. He said that digitalin is very slowly absorbed by the frog, whereas the pigeons are quickly responsive. The point he wanted to make, however, was that a decision should be reached on method to be adopted.

James C. Munch said that the Committee on Physiological Assays A. PH. A. is now engaged in a somewhat similar study. Approximately fifty gallons of tincture of digitalis had been prepared and submitted to bio-assayists of the ASSOCIATION for comparative assays and to clinicians for study. He had been collecting various methods for the assay of digitalis, and now had about fifty-seven methods; so far none of the studies by clinicians have been completed, but a study is under way. He stated that Rowe's study represented about a year's hard work. He conducted work of this kind several years ago with the view of determining the accuracy of the 1-Hour Frog Method. In writing to the assayists he had requested that they use the 1-Hour Method

and report on other methods which they had employed; also information was requested relative to the experience of the assayists.

In discussing the subject with Dr. Hanzlik in Boston, he had been informed that Dr. Hanzlik would publish the results he had obtained in several kindred clinical cases compared with the "pigeon emesis" method.

W. H. Zeigler stated that he had studied one of the assays and he was looking forward with interest to the clinical reports.

E. Fullerton Cook referred to the efforts being made to establish international standards. He stated that there will be an International Secretariat on Pharmacopœias under the auspices of the League of Nations where every nation may obtain definite standards.

James C. Munch stated that he had quite a lengthy discussion with bio-assayists of Canada while in Boston. They have been using "International Standard" leaf and obtained quite uniform results. They pointed out to him that it was necessary to specify in greater detail the method of preparing the test solution because slight variations in technic will give results varying from 25 to 100 per cent.

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p_H STUDIES OF NEOARSPHENAMINE.*

BY RALPH B. SMITH, A. E. JURIST AND W. G. CHRISTIANSEN.

Work done in this laboratory by Jurist and Christiansen[1] indicated that it would be desirable to determine the p_H of neoarsphenamine solutions, since the very rough results obtainable with indicators had given considerable evidence that the stability of the product was related to the p_H of its solution. Furthermore the p_H could be used to indicate the presence of free acid because both sodium formaldehyde sulphoxylate and 3,3′-diamino-4,4′ dihydroxyarsenobenzene-*N*-methylene-sodium-sulphinate have a p_H of more than 8.0. Williams and Swett[2] state that they have determined the p_H of solutions of a number of commercial neoarsphenamines but give no details as to the method employed. Elvove and Clark[3] and Hunter and Patrick[4] have investigated the p_H of arsphenamine solutions with the hydrogen electrode and found that true and reproducible values could be obtained and it was found in our Laboratory that the method of Elvove and Clark could be adapted to neoarsphenamine.

In this investigation a bubbling type of electrode was used with a saturated half cell of the type described by Clark and Cohn.[5] The electrodes were prepared according to the method of Elvove and Clark[3] by first plating them with a thin layer of bright gold and then with a thin layer of palladium black. Electrodes of both the coil and point type were used but as far as could be noted there was no difference between the behavior of the two types; in all cases a fresh pair of electrodes was used for each determination.

The general method was to put 13.5 cc. of double distilled water which had been cooled under nitrogen into the electrode vessel, place two electrodes in position and pass hydrogen through the bubbling tubes for about fifteen minutes,

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* Scientific Section, A. PH. A., Portland meeting, 1928.

[1] *J. A. C. S.*, 50 (1928), 191.

[2] "Proc. Soc. Expt. Biol. Med.," 19 (1922), 266.

[3] Hygienic Laboratory—Bulletin No. 135.

[4] *J. Lab. & Clin. Med.*, 10 (1925), 343.

[5] "Public Health Reports," 38 (1923), 933.

so as to saturate the electrodes and the water. At the end of this time the electrodes and their bubbling tubes were raised about two cms. above the surface of the water, the electrode vessel removed without stopping the hydrogen flow and 2.7 Gm. of neoarsphenamine sprinkled on top of the water. The tube was now put back into position and the neoarsphenamine allowed to dissolve. It was found that in most cases the powder would dissolve without stirring but where this was necessary it was accomplished by a small stirring rod passed through the hydrogen outlet. When the neoarsphenamine powder comes in contact with the electrode surface it increases the time necessary for the electrode to come to equilibrium and also increases its tendency to poison, however, the method of manipulation just described prevents this from happening. As soon as all the neoarsphenamine was dissolved, the electrodes and their bubbling tubes were lowered into the solution and the whole apparatus lowered into the constant temperature bath. The neoarsphenamine solution was protected against the entrance of air by trapping the exit hydrogen through about one cm. of water. The effect of hydrogen on the solution both in the presence and absence of the electrodes was studied by means of the iodine titration method, thus measuring any possible change in reducing power due to oxidation, and it was found that the protection of the solution by hydrogen was equal to or better than that afforded by nitrogen which is usually assumed to completely protect these solutions. The following table gives one set of results obtained in comparing the protection to the solution by hydrogen and nitrogen as determined by drawing a sample equivalent to 0.10 Gm. from the solution under examination and titrating with $N/10$ iodine.

PROTECTION OF NEOARSPHENAMINE SOLUTIONS BY INERT GAS.

Time.	$N/10$ iodine used.		Per cent loss.	
	Sample under H_2, cc.	Sample under N_2, cc.	Under H_2.	Under N_2.
0 hrs.	17.08	16.80	0.0	0.0
4	16.83	16.27	0.2	0.42
$22^1/_2$	16.38	15.26	0.56	1.23

This table shows that the loss under H_2 in four hours is within the limit of experimental error.

It was found in most cases that the electrodes came to equilibrium with each other and remained constant within one or two millivolts in 15–30 minutes. The electrodes were then watched for about 30 minutes longer. They generally remained constant within two millivolts during this period or dropped off slightly. In all determinations the highest electrode reading was taken in calculating the p_H. This value was used because it was found that this point was generally reproducible within 0.05 of a p_H unit by different operators and at widely separated times. It should be noted in connection with the above that neoarsphenamine solutions appear to be on the border line of solutions which poison electrodes and those which do not and a number of experimental samples have been tested which poison the electrode so badly that no reliable readings could be obtained. This was more frequently noticed in samples having a p_H below 7.5. Electrodes used in neoarsphenamine solutions have, however, been repeatedly checked against $N/20$ potassium acid phthalate and in all cases where otherwise satisfactory readings have been obtained, the phthalate check usually gave readings within

2–3 millivolts of the correct value. It should be remembered, however, that where a voltage of 0.481 was not obtained these same electrodes had usually started to show a drop from their high value in the neoarsphenamine solution; this is another reason for using the highest potential registered by the electrode in the neoarsphenamine solution when calculating the p_H. A rapid drop after a brief maximum was considered as a strong indication of poisoning and that at the maximum voltage the electrode had not reached true equilibrium.

The experimental results given in the following tables are divided into three groups. The first table gives a series of determinations in duplicate intended primarily to show how closely it is possible to check duplicate determinations on different types of neoarsphenamine. It further shows the effect of dilution on the p_H.

TABLE A.—CHECK DETERMINATIONS OF p_H ON DIFFERENT TYPES OF NEOARSPHENAMINE.

Sample no.	p_H 20% sol.	p_H 4.5% sol.	Electrode voltage in voltage in $N/20$ phthalate.
A	6.99	7.30	Not tested
	6.98	7.25	0.447
	6.94	..	Poisoned on dilution
B	6.32	6.62	0.476
	6.31	6.65	0.480
C	7.87	8.14	0.480
	7.83	7.96	0.480
D	8.32	8.41	0.480
	8.32	8.46	0.481
E	8.66	8.82	0.480
	8.67	8.77	0.480

These results show that the maximum variation, with one exception, is 0.05 p_H units which is within the limits of experimental error with this type of material. On dilution from 20% solution to 4.5% the p_H has shown an increase of from 0.09 units to 0.34 units in the results given but increases as high as 0.45 units have been observed. One commercial sample has been found which, when diluted from 10% to 2.5%, decreases in p_H from 8.50 to 8.39. We have no evidence to explain this dilution change but two apparent explanations are either a change in the colloidal state of the solution or a depolymerization of the dissolved arsenical.

The results given in the following, Table B, show that the p_H on dilution rises steadily from a concentration of 40% neoarsphenamine to 0.1%.

TABLE B.

Concentration by weight, %.	p_H.
40	7.60
20	7.73
10	7.78
2.5	7.88
0.5	8.50
0.1	8.62

These results indicate that the effect of dilution is in the same direction over a very wide range of concentration.

Tables C and D give a series of determinations on experimental and market neoarsphenamines showing the wide range of p_H covered by these products.

Table C.—Values Obtained with Different Types of Experimental Neoarsphenamines.

Class.	p_H in 20% sol.
A	8.01–8.74
B	6.31–6.99
C	7.62–7.87
D	6.62
E	8.04
F	6.74
G	7.01
H	6.99
I	7.97

Table D.—p_H of Market Brands of Neoarsphenamine.

Sample no.	p_H in 20% sol.
A	5.78
B-1	8.30
B-2	8.07
C	8.48
D	8.20

The results show a range of 6.31 to 8.74 for the experimental preparations and 5.80 to 8.48 for the market samples.

SUMMARY.

1. The method of Elvove and Clark for the determination of the p_H of solutions has been successfully applied to neoarsphenamine.

2. The range of p_H for different types of experimental and commercial neoarsphenamine is shown.

3. The effect of dilution on the p_H of neoarsphenamine solutions is indicated and two possible explanations are suggested.

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MEDICINAL WOOD TAR CREOSOTE: I. METHOXYL CONTENT AS A CRITERION OF THE COMPOSITION OF CREOSOTE.*

BY DARRELL V. SICKMAN[1] AND ROBERT P. FISCHELIS.

Wood tar has been used for one purpose or another since the dawn of recorded history. The Egyptians used it to preserve their mummies and the preservative action of "wood smoke" has been made use of in various industries, from the earliest times to the present day. Reichenbach (1), in 1832, determined that the antiseptic properties of wood tar resided in the alkali-soluble portion of this crude material and he named this particular fraction "Kreosot."

For a long time creosote was confused with phenol (2) which was discovered as a constituent of coal tar by Runge, in 1834. Early investigators considered creosote to be a chemically homogeneous substance and tried the effect of oxidizing agents, chlorine, metallic potassium, sulphur, etc., upon it. However, these experiments shed very little light upon the constitution of creosote.

That creosote is not identical with phenol was first shown by von Gorup-Besanez (3) in 1841. In 1858, Hlasiwetz (4) established the fact that creosote contains guaiacol and creosol, which was later confirmed by Müller (5). An account of all work done on creosote up to 1867 is given in an interesting article by

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* Scientific Section, A. Ph. A., Rapid City meeting, 1929.

[1] Maltbie Chemical Company Research Fellow, Princeton University, 1928–29.

von Gorup-Besanez (6). In 1869 Max Biechele (7) again analyzed creosote, and in the same year Marasse (8) showed that other phenols besides guaiacol and creosol were present in creosote. The higher boiling phenols were extensively investigated by A. W. Hoffmann (9) and Liebermann (10), who showed that these were derivatives of pyrogallol. Tiemann (11), the discoverer of vanillin and the ionones, with his students carefully examined creosote, and established the structure of creosol.

Pastrovich (12) isolated an interesting phenol from creosote which he called cœrulignol. It is considered exceedingly caustic and toxic, a drop placed on the tongue causing bleeding. A characteristic blue color is produced when cœrulignol is treated with barium hydroxide, and nearly all the pharmacopœias list the application of this test to creosote to insure the absence of cœrulignol. Pastrovich considered cœrulignol to be 4-*n* propyl guaiacol; but pure *n*-propyl guaiacol formed by the reduction of eugenol shows none of these properties, so that the nature of this substance must be regarded as unknown.

Kebler (13) reported on the examination of six commercial samples of creosote in 1889, and describes a method for estimating guaiacol in creosote. A thorough study of creosote was not made until 1894 when Béhal and Choay (14) made a more or less quantitative investigation of official creosotes and isolated a number of new phenols from creosote. Very little chemical work has been done on creosote in the lasty thirty years, with the exception of an examination of the pyrogallol derivatives of maple creosote and the isolation of a new phenol, 4-vinyl guaiacol.

COMPOSITION OF CREOSOTE.

The known constituents of crude wood tar creosote are as follows:

Phenol (3*c*), (6), (8), (11*c*), (14)
Ortho, meta and para cresols (3*c*), (6), (8), (11*c*), (14)
Ortho ethyl phenol (14)
1,3,5-xylenol (14)
1,3,4-xylenol (8), (14), (11*a*, *b*)
Pyracatechol (5)
Guaiacol (3*c*), (6), (13), (14)
Creosol (4), (13), (14)
4-ethyl guaiacol (14)
4-vinyl guaiacol (16)
4-*n*-propyl guaiacol (12)
Pyrogallol dimethyl ether (9), (15)
Methyl pyrogallol dimethyl ether (9), (15)
Propyl pyrogallol dimethyl ether (9), (15)

The derivatives of pyrogallol are highly toxic, and are carefully removed from medicinal creosote.

A detailed analysis of official French beechwood creosote boiling between 200° and 210° is given by Béhal and Choay (14*b*) as follows:

Phenol	5.2
1–2 cresol	10.4
1–3 and 1–4 cresols	11.6
1–2 ethyl phenol	3.6
1–3–4 xylenol	2.0
1–3–5 xylenol	1.0
Phenols, various	6.2
Guaiacol	25.0
Cresol and its homologs	35.0
	100.0

The same authors give the following as the comparative composition of beech and oak creosotes:

	Beech.	Beech.	Oak.
Distillation range, °	200–220°	200–210	200–210
Specific gravity	1.085	1.085	1.068
Monophenols	39.0	39.0	55
Guaiacol	19.7	26.5	14
Creosol and its homologs	40.0	32.1	31
Loss	1.3	2.4	....

The most important conclusions which can be drawn from these results are that the proportion of guaiacol in creosote is far smaller than is ordinarily assumed, some authors stating that creosote is 90% guaiacol. It would also seem that all the guaiacol, as well as a considerable proportion of the creosol present, distil below 210°. The oak creosote apparently contains less guaiacol and more monophenols than the beechwood, but this is fortuitous, as the specific gravity of the oak creosote is far below U. S. P. standards, while that of the beechwood creosote is unusually high. As the specific gravity of phenol is 1.065, the cresols about 1.04 and that of guaiacol is 1.14, it may be said in general, that the higher the specific gravity of a sample of creosote the greater is the proportion of guaiacol and creosol it contains.

The desirability of securing accurate information on the actual guaiacol and creosol content of creosote is obvious and becomes of particular importance to manufacturers of medicinal preparations which depend largely upon their creosote content for therapeutic effect. Up to the present time, very little experimental work has been done on the pharmacology of the individual constituents of creosote. It is therefore impossible to ascribe the therapeutic effect of creosote to any single constituent or group of constituents of creosote. It is likewise difficult to accept or reject any sample of creosote meeting U. S. P. requirements, on the ground that it is high or low in content of a single constituent or several constituents. It is generally assumed, however, that an appreciable percentage of guaiacol and creosol is essential to assure medicinal value. Proceeding on that assumption it would appear to be essential to provide a quantitative estimation for guaiacol and creosol in creosote.

EXPERIMENTAL.

Although a few methods have been proposed for determining guaiacol in creosote, it was found impossible to obtain reliable or consistent results with them. As guaiacol and its homologs contain a methoxyl group, which is easy to determine quantitatively, it was thought that the methoxyl content of creosote would give a valuable criterion of the proportion of these substances present in the sample. It should be pointed out that, owing to the difference in the molecular weights of guaiacol and creosol which make up the bulk of the dihydroxy phenols present, and the fact they are present in relatively variable proportions, it is not possible to calculate exactly either the amount of each present or of both taken together.

The method used was that of Hewitt and Jones (17), using pyridine to absorb the methyl iodide. The apparatus used was that of H. Meyer (18) but nitrogen instead of CO_2 was used to carry the methyl iodide over into the pyridine. The absorption apparatus was that of Pieper, Acree and Humphrey (15), and gave com-

plete satisfaction. A less elaborate apparatus would doubtless give just as good results. In this method, the sample is heated with concentrated hydriodic acid in a stream of nitrogen. The hydriodic acid breaks the $\equiv C—O—CH_3$ grouping, forming methyl iodide. The nitrogen is bubbled through pyridine, which absorbs the methyl iodide quantitatively and converts it into an easily ionizable combination. When the reaction is complete, the pyridine is poured into a measured volume of $N/10$ silver nitrate, acidified and the excess silver determined by Volhard's method. A determination may be made in $1^1/_2$ to 2 hours.

The results of work on sixteen samples of creosote are given in the table.

DISTILLATION OF CREOSOTE AT DIFFERENT TEMPERATURES AND PERCENTAGES OF GUAIACOL AND CREOSOL.

		Volume of Distillate from 100-cc. Sample. between Degrees C: Mentioned										
Sample no.	Sp. gr.	Below 200°C.	200° to 205°	205° to 210°	210° to 215°	215° to 220°	200° to 210°	210° to 220°	200° to 220°	W.	X.	Y.	Z.
1	1.0751	0	30	24	14	16	54	30	84	11.22	44.9	49.9	C
2	1.0790	0	16	39	21	15	55	36	91	12.22	48.9	54.4	C
3	1.0772	0	20	37	21	13	57	34	91	11.98	47.9	53.3	C
4	1.0771	0	15	40	23	13	55	36	91	11.94	47.8	53.1	C
5	1.0746	0	10	43	24	15	53	39	92	10.98	43.9	48.9	C
6	1.0804	0	0	23	43	21	23	64	87	13.07	52.3	58.2	N
7	1.0780	0	0	36	35	20	36	55	91	12.60	50.4	56.1	N
8	1.0830	0	10	47	24	13	57	37	94	13.20	52.8	58.2	N
9	1.0834	0	3	43	28	16	46	44	90	13.24	53.0	58.92	N
10	1.0781	0	20	36	23	14	56	37	93	12.37	49.5	55.2	N
11	1.0816	0	0	10	51	23	10	74	84	16.30	65.2	72.6	N
12	1.0800	0	5	45	28	14	50	42	92	13.96	55.8	62.8	N
13	1.0802	0	9	41	27	15	50	42	92	14.50	58.0	64.5	N
14	1.0827	0	3	29	31	18	32	49	81	14.20	56.8	63.2	N
15	1.0782	0	5	41	27	14	46	41	87	12.70	50.8	56.5	N
16	1.0731	0	3	34	26	19	37	45	82	12.25	49.0	55.6	N
U. S. P. X Standard	1.076								90				
B. P. Standard	1.080								75				

Explanation of abbreviations: W—Methoxyl per cent; X—Methoxyl calculated as guaiacol; Y—Methoxyl calculated as creosol; Z—U. S. P. Glycerol test; C—Clear solution; N—Normal.

All samples of creosote were obtained on the open market, and all samples except 14, which was a semi-refined creosote, and 16, which was marked B. P. 1882, were offered as U. S. P. Only 15 and 16 are beechwood, the others apparently coming from a mixture of hardwoods. The specific gravity, distillation data, and glycerol tests were made according to the U. S. P. X. All the samples behaved normally in the other U. S. P. tests. The U. S. P. X requires a specific gravity of not less than 1.076 and that not less than 90% by volume shall distil between 200° and 220°.

Most of the samples examined were of good quality as judged by the U. S. P. standards. Sample 11 is apparently the residue left after the guaiacol had been removed, and is mostly creosol. The methoxyl content is roughly in the same order as the specific gravity. Apparently the U. S. P. requirements of specific gravity and distillation range are sufficient to insure a methoxyl content of 11% or more, corresponding to a guaiacol and creosol content of 44–49 per cent.

It is quite apparent from these results that creosote is only about one-half

guaiacol and creosol, and as there is at least twice as much creosol as guaiacol present, according to Béhal and Choay's work quoted above, guaiacol can scarcely be the principal ingredient of medicinal creosote.

As the table shows, creosote varies widely in composition, and unfortunately most of the tests devised for ascertaining its quality are valueless. If the dihydroxy phenols are assumed to be the medicinally active ingredients, a methoxyl determination will indicate the proportion of them present far more accurately than any method of which the writers have knowledge. The methoxyl determination is rapid and inexpensive, and if used in conjunction with the distillation test of the U. S. P. and the specific gravity, leaves no doubt of the composition of the creosote. Creosote is an extremely complicated mixture and this simple method of evaluating it should not be ignored.

We desire to express our thanks to Professor Gregg Dougherty of Princeton University for his kindly interest and very helpful suggestions with regard to the general problem of creosote chemistry, and particularly the experimental phases reported in this paper. The experimental work has been done under the 1928-29 Maltbie Chemical Company Fellowship for Creosote Research at Princeton.

SUMMARY.

1. A brief history of the chemical examination of creosote is given.

2. The composition of medicinal creosote is discussed, and its difference from guaiacol is pointed out.

3. A simple method (not new) of determining the methoxyl content of creosote is given and its importance in evaluating creosote is discussed.

4. A number of creosote samples from the open market have been examined in the light of the U. S. P. tests and methoxyl content.

5. It is shown that approximately 50% of medicinal creosote consists of derivatives of pyrocatechol, and that there is no distinction between beechwood and other hardwood creosotes.

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A PRESCRIPTION CONTAINING GUAIAC AND ACACIA.*

BY JOHN C. KRANTZ, JR., AND C. JELLEFF CARR.

INTRODUCTION.

Mixtures containing the resinous tincture of guaiac have occupied a prominent place in the teaching of prescription incompatibilities for many years. The proper compounding of prescriptions containing various quantities of tincture of guaiac, honey, acacia, potassium chlorate and water require an exercising of the pharmaceutical art of compounding. From a retail pharmacy in Baltimore the following prescription was brought to the attention of one of the authors:

Tinct. Guaiaci	15
Mel Depurati	15
Kali Chlorati	13
Syr. Acaciae q. s.	90
Misce et pone in solutio	

This prescription had been compounded several times according to the generally excepted procedure, producing upon each occasion the characteristic pinkish red coloration of a guaiac mixture. The next time the prescription was filled, presumably in the same manner as before, the mixture developed during the course of compounding a bluish green color. Four additional attempts at compouding, modifying the methods of mixing with the same ingredients, produced the bluish green color.

The authors decided to subject the mixture to a scientific investigation in order to determine the nature of the color change.

HISTORICAL.

The pharmaceutical literature is replete with records of work which has been carried out in studies of the constituents of guaiac and some of its color reactions. E. Schaer (1) determined that guaiac resin contained 70 per cent of guaiaconic acid and 10 per cent of guaiacresinic acid. The former produces the characteristic blue with oxidizing agents, whereas the latter does not react in this way. This same investigator observed that the exposure of guaiaconic acid to sunlight brought about a molecular rearrangement of the compound rendering it inactive in the presence of oxidizing agents. Atkins (2) observed that certain metallic ions interferred with the guaiac test for oxidases by reacting with the guaiaconic acid to produce the blue color thus vitiating the test. Sartory (3) confirmed the observations of Atkins pointing out that potassium permanganate and cupric salts reacted with guaiaconic acid to produce the characteristic blue color. Schaer (4) observed that alkalies and alkali-carbonates decolorize guaiac-blue and prevent its formation, which he believes to be an ozonide of guaiaconic acid.

A recent study of acacia by Tschirch and Flück (5) has shown this gum to contain certain oxidases. The Pharmacopei Helvétique makes provisions for the destruction of the oxidase in the gum by the boiling of a solution of the product for ten minutes. Various methods of inactivating the oxidase were described

* Section on Practical Pharmacy and Dispensing, A. PH. A., Rapid City meeting, 1929.

recently by M. Mascré (6), these consist essentially of boiling the aqueous solution of the gum or treating the dry gum for one hour with boiling salcohol.

EXPERIMENTAL.

This prescription was compounded with a powdered gum arabic of U. S. P. quality. The characteristic blue color developed. The hydrogen-ion concentration of the mixture was measured electrometrically by means of the quinhydrone electrode. The p_H of the mixture was 4.42. The mixture was prepared omitting the potassium chlorate and the blue color appeared as before. Including the potassium chlorate and omitting the acacia, no blue color developed, likewise it was shown that honey was not responsible for the color change. This seemed to indicate that acacia was responsible for the oxidation of the guaiaconic acid.

The prescription was compounded with all of the ingredients in addition to 1 per cent hydrochloric acid—the p_H of this was 0.48 and no blue color developed indicating that in a high hydrogen-ion concentration the oxidase is inactivated. In order to ascertain the influence of a solution containing a lesser hydrogen-ion concentration, the mixture was prepared in 0.01 *N.* hydrochloric acid and 1 per cent acetic acid, respectively. The p_H of the former was 3.32 and that of the latter was 3.71. In neither of these products did the blue-green coloration appear indicating the inactivation of the oxidase with these degrees of hydrogen-ion concentration.

The mixture was prepared containing 1 per cent potassium bicarbonate, 1 per cent potassium carbonate and ammoniated tincture of guaiac, respectively.

With $KHCO_3$	—	p_H about 8.4
With K_2CO_3	—	p_H about 11.6
With NH_4OH	—	p_H about 11.3

Not any of these products developed the blue color, however, the usual pink coloration was replaced by a brown color. This confirms Shaer's observation that alkalies prevent the formation of the guaiaconic acid oxidation product.

The solution of acacia was boiled for fifteen minutes before introducing it into the prescription. No blue-green color developed which indicated the inactivated oxidase as described by Mascré. This was repeated several times and in none of these mixtures did the oxidation of guaiaconic acid occur.

In order to ascertain the influence of boiling upon the hydrogen-ion concentration of the acacia solution, 6 Gm. was dissolved in enough water to prepare 90 cc. The p_H of this solution, measured by means of the hydrogen electrode, was 4.45. This value is in close agreement with the work of Schwartze *et al.* (7) and that of the first author (8). The solution was boiled for twenty minutes, allowed to cool, and the hydrogen-ion concentration was measured. This value was p_H 4.42. This experiment indicates that boiling does not influence the p_H of the acacia solution and it is not this reason that boiling prevents the formation of the blue-green color.

Considering the conclusion of Shaer, that guaiaconic acid underwent molecular rearrangement upon exposure to light and became inactive in the presence of oxidizing agents, the following experiment was performed. A sample of tincture of guaiac was exposed to ultraviolet light (Alpine Sun Lamp 12 inches from the

mercury arc in quartz) for a period of thirty minutes. This sample as well as a control were used to prepare the guaiac-mixture prescription. In each the blue-green color developed simultaneously and approximately to the same degree. From the work of Shaer one might have expected this treatment with ultraviolet light to prevent the formation of the oxidation product of guaiaconic acid. Under the conditions mentioned, the authors found no influence upon the color formation after irradiation with ultraviolet light.

CONCLUSIONS.

1. The blue-green color formed in the mixture described in this paper is due to the action of the oxidase in acacia upon one of the constituents in tincture of guaiac.

2. The oxidation and accompanying color change can be prevented by inactivating the oxidase in acacia by boiling a solution of the gum for twenty minutes.

3. Modifying the mixture so as to change the hydrogen-ion concentration to a p_H below 3.71 or above 8.4 prevents the formation of the blue-green color.

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ABSTRACT OF DISCUSSION.

In reply to the question by **John Culley,** what the objection was to the green color—**Dr. Krantz** stated that he did not investigate the therapeutic activity, but the patient did not accept the refilled prescription, because the color of the preparation was not like that of the first preparation.

E. Fullerton Cook thought the difference in color was due to the age of the preparation.

C. M. Snow inquired how far a pharmacist could go in making changes that would not affect the therapeutic activity. He asked to be informed on the subject under discussion—as acacia is the disturbing factor, the component being syrup of acacia; also, as powdered acacia, usually, does not contain the ferment—whether substitution of simple syrup for syrup of acacia would be permissible.

William Gray inquired whether Dr. Krantz considered that the guaiac had a part in the variation of color reaction.

Dr. Krantz replied that three different guaiacs were used in an effort to obtain the coloration of the first preparation—one from the original sample; one an old guaiac, purchased from a retail pharmacist; and another from a fresh sample. Invariably a greenish color was obtained, with slight difference in shade. The greenish color developed when the acacia solution was not heated, but not when the solution was boiled—the color varied in degree of intensity.

William J. Husa expressed the opinion that the oxidase had no therapeutic value in the preparation and, hence, no harm is done by destroying the ferment as far as medicinal value is concerned; but if the acacia is left out of the prescription there would be a change in the preparation which might not be permissible.

A. O. Mickelsen questioned the right to destroy the oxidase and thus change the prescription.

PHARMACEUTICAL RESEARCH LABORATORY,
SHARP AND DOHME.

THE NEIGHBORHOOD STORE—HOW TO TRAIN FOR IT.*

BY WORTLEY F. RUDD.

The implication in the subject is that there is a difference between the requirements for a successful neighborhood pharmacist and the man in a metropolitan district. I think there is. Further, I am assuming in the selection of the subject that in the main the neighborhood store will continue to be independently owned. This too, I think, will probably be true—certainly in that section of the country with which I am most familiar.

With these two as my chief assumptions then, let us analyze quite critically what personal qualities and what sort of training are required that our neighborhood pharmacist may make himself so indispensable to his constituency and at the same time such a good business man that his place as an independent is permanently fixed in both the economic and social scheme.

I shall include the small-town druggist, of course, in what I have elected to call the neighborhood druggist. Taken by and large, the owner of our neighborhood store knows by name a very large majority of his customers. He knows their individual tastes and their potential buying power. He knows, in many instances, their family problems, health conditions, business relations and personal habits; in fact, I am inclined to the belief that he at least has the opportunity of knowing more about those who come to him for service than does any other community member—not excepting the physician and the minister.

If these things be true, and most of them I believe are generally conceded to be, his requisites for success are a composite of sound intelligence, good judgment, business acumen, fundamental training, good health, industry and a pleasing personality—a large order to be sure, but a real deficiency in any one of them is often his undoing.

It is manifest then, that the most important single step in preparing men for successful neighborhood proprietorship is in finding the right sort of high school graduates who may be interested in such work. Frankly, this is a very difficult task. Often the boy, who gives evidence of a reasonable share of the essential qualities enumerated, cannot even be induced to think seriously of pharmacy as his life's work. Little wonder that this is true. At present the demands of pharmacy are manifestly too great for its compensations. I am aware that this is a rather unusual statement to come from one in administrative charge of a state school of pharmacy. Right here I want to say that if I believed for one minute that this condition was inherentiy a part of pharmacy and would therefore continue, I would be unfair to myself and to those young men and women who come into our school to encourage them to remain in pharmacy.

This is tantamount to saying what all of you must know, *viz.*, this pharmaceutical generation, the one to which you and I belong, with its economic, legal and educational pressure, must resign itself to a sort of vicarious existence that such intolerable conditions may not be passed on to those that are to come after us.

The neighborhood druggist! What will be his status in 1960? I venture to say that the answer to the question is almost, if not wholly, in the hands of those en-

* Section on Education and Legislation, A. PH. A., Rapid City meeting, 1929.

trusted with the selection of the right men, giving them the right sort of cultural and professional education and inculcating in them the proper point of view about pharmacy—its opportunities, obligations and social significance.

Coming then directly to the subject of this paper—"How shall we train the neighborhood druggist?"

In the first place, and I repeat this, the selection of the right sort of men is of primary importance. This is a joint responsibility—the present retail pharmacist, the travelling man and the jobber all may help the schools in making these selections. Practically every young man making application for admission is known personally to one or more of the above. Cutting off the unfit right at the source must be done ruthlessly. I doubt that this is being done as it should be.

Once in training, what shall we do for him? Certainly not what the average school is doing for him now. The graduate in pharmacy of to-day is well trained neither in business nor professionally, nor is he given the culture which his position demands. I hold that the neighborhood druggist of the future must have all of these—another large order—but I believe it is imperative.

I often wonder just what were the determining factors in the decision to go to a four-year course in pharmacy. In some states—my own, for example—this may cut down the number of students to an almost dangerous minimum, and yet in spite of this prospect, we have committed ourselves to it. Why have we done it? Isn't it due to a slow but steadily growing conviction that the chances for the ultimate survival of the independent are directly proportional to the lifting power of the training we of the schools give him?

It seems to me then, that with this prospect before us, any sort of detailed discussion of this training would be superfluous. The point I hope to make is that in going from the two-year course to the three and then to the four, we are recognizing the utter inadequacy of the old, and are therefore discarding it for an opportunity to do something for men of the next generation which may save them from a repetition of what we have seen and are seeing now. Would any of us have our own sons trained for the pharmacy of to-day? Have our schools of pharmacy on the average yet any sort of conception of this larger view of pharmaceutical training? Even granted the vision on their part, are our faculties well qualified to do the job? In a study made a year ago and presented to this Section on "Professors of Pharmacy," the inadequate training of many men holding this, the most important chair in our schools, was, I think, clearly proved. But why run on any longer? I find it exceedingly difficult to get anywhere in this paper. I would not have written it, however, if I were not firm in the belief that there is a way out. I am not alone in the position I take. I think most of us are in a sort of maze. I wonder if it is not well that we are not cocksure of ourselves in this connection! I am wondering if this uncertain state of mind is not a hopeful sign. I venture to raise the inquiry—wouldn't we be further along now if this sort of spirit had been prevalent earlier in the history of our educational problems? I have no answer to my own inquiries—probably you have.

May I sum up then, in a single paragraph, all that I have tried to say in the foregoing paragraphs?

The kind of training we have given our pharmacists during the past generation and right on into this one is as much responsible for our present chaotic condition

as any other one thing. Further, to save the independent at all, from now on his education must make him just as cultured, just as broad, just as adaptable, just as skillful as any other group in the complex community life in which he is to serve. Education, and not legislation, is, I believe, his only way out.

ABSTRACT OF DISCUSSION.

James H. Beal, in discussing the paper, stated that for a number of years pharmacy has been scattered all over the shop and it was questioned whether all parts could be put together again. There had been times when he had been almost hopelessly discouraged, but he did not feel that way any more; the type of young men going into pharmacy had encouraged him. He referred to Benjamin Franklin's remarks at the conclusion of the Constitutional Convention in 1787—he had been wondering whether the sun on the back of the President's chair was a rising or setting sun—with the successful conclusion of the day's work Franklin believed it to be a rising sun; so the speaker felt, because of the incoming young men and women that the sun of pharmacy is rising.

Rudolph H. Raabe agreed with the foregoing speaker that pharmacy was progressing.

THE RETAIL DRUG STORE A NATIONAL NECESSITY.*

BY R. E. LEE WILLIAMSON, BALTIMORE.

I believe there is no one in this audience who will dispute the statement made by me in the title of this paper. I believe that anyone who will give the matter a moment's serious thought, be he a layman or a pharmacist, will confirm the statement that the Retail Drug Store is a national necessity. That being accepted, why should I presume to present, to you of all men, an address which has for its purpose, judging from its title, an effort to influence you to accept the fact set forth as being a fact when you have no contrary opinion.

Let me, at the very start, assure you that I have no such intention. It is, however, my purpose to proceed immediately on the basis that you are convinced beyond any doubt that one of the vital necessities of the nation is the Retail Drug Store; and then, if possible, to arouse in you a keen sense of responsibility, and through you as leaders in pharmacy, this sense of responsibility in other members of our profession, so that this necessary service of the Retail Drug Store to the people of the Country will be preserved and improved that it may meet the requirements of the ever changing conditions and customs of living. To preserve the Retail Drug Store and improve it, there must be, on the part of every pharmacist, a willingness to look squarely in the face the changes that are constantly taking place in the business methods of our day and time; to face these changes without prejudice—with a determination to adjust our business to them; not trying to accomplish the impossibility of fighting against a modern trend.

I am convinced that the Independent Retail Drug Store can maintain its position of respect and confidence in the mind of the public—preserving its professional standing as a pharmacy and at the same time conducting a retail drug business on a dignified modern and profitable basis. But, to accomplish this, there must be given an open-minded consideration of the modern methods of conducting the retail business. We must clearly understand that new methods are adopted because of the demands of the people and the necessities of the times. They are

*Section on Commercial Interests, A. PH. A., Rapid City meeting, 1929.

not put into effect to suit the ideas of a radical merchant. They are put into effect, however, because the forward-looking merchant is alive to the wisdom of meeting the requirements of the public and catering to its needs in the manner that is not only attractive to it, but is demanded.

For many years the professional and scientific side of the retail drug business has been alert to the opportunities of pharmacy and has advanced in its methods and procedures—it is not of this side of the retail drug business that we are concerned in this address—it is of the business side of the retail drug store that the serious-minded retail druggist is concerned—in fact, many are alarmed, and it is to this condition that I am hoping to direct your thoughts. To-day the retail drug store, as a unit of retail distribution of merchandise, covers a wide expanse—it is most elastic, its confines are anything but rigid—however, that is not a new condition—forty or more years ago, the drug store was bounded on one side by quinine and castor oil and on the other side by paints and window glass and to-day these boundaries are on one side antitoxins and animal glands to mystery novels and electric coffee pots on the other. This condition for our purposes is immaterial for always there has been and will be a proper and dignified middle ground. Such conditions are not problems of a serious or vital nature as they are dependent upon the whims and tastes of an individual. All of the drug stores that have been started and all that will be started, have just two foundations to build upon. The first of these is the foundation of the Prescription Department where all else is secondary when it in any way detracts from the importance of that department. The second is the foundation of merchandise handled and sold, without regard to its effect upon the Prescription Department and the profession of pharmacy, in fact, making pharmacy secondary.

Built from the first foundation will grow a real retail drug store; built on the second foundation will grow an Oriental bazaar labelled "Drug Store"—but the public will know.

How can the independent retail drug store maintain itself in this day of intensive competition? In approaching that angle, let us call things and people by their right names—not in an ugly manner or spirit, but rather in a manner careful not to give the impression that we are antagonistic, but that we are simply trying to intelligently discuss and analyze an established condition.

When we look over the period of the last thirty years in the retail drug business, to my mind, there are three things that stand out: Price Cutting, Price Maintenance Laws, Chain Stores. What influence have they had in the past and what do they mean in the future for the Independent Retail Druggist?

To-day, there is no such thing as price cutting. When everybody does the same thing, then that practice becomes the established standard.

Price cutting is now leveled down to what you might call a level of prices. They fluctuate up and down—they may be eighty-nine or seventy-nine, but the main level is there and must be accepted, because the public has been educated to that level of prices.

The price maintenance law has not, so far as I can see, accomplished anything yet for the good of the durggist. I am frank to confess that we are further ahead toward probably getting a price maintenance law in the Kelly-Capper Law than we have ever been. I hope to see the day when that bill will be passed and then

we will be able to see its benefits and services. Up to the present time it has accomplished, as an influence on our business, nothing, except to retard us, because it has clouded our vision to the other things to which we should have turned our attention, that we should have spent our money for and that we should have had our minds actively engaged in. Had we spent half the time, half the money and half the energy in trying to meet in the retail drug store the modern method, the accepted method of conducting a retail business, we would have been further ahead than we are to-day. The effect it has had on the independent retail druggist is just as I have said. It has retarded his progress as a modern storekeeper.

THE CHAIN STORE.

What has the chain store done and what is the chain store? The chain store was simply a natural growth in the first place of some ambitious retail druggist who saw he had energy and ability enough to manage more than one store.

It is not so very difficult to manage two stores. It is not a difficult trick to manage three stores, and so on as we go in ascending progress. The chain store was simply the development of man's ambition to expand his business. Those were the individual chains, local chains, but then what happened? Then came the national chain. What was the origin of their growth? Why did they grow? They grew because a group of men or a man saw an opportunity to expand the retail drug business to meet the modern tastes and requirements and demands of the consuming public, and that was made possible by the negligence of the retail druggist himself.

You can look back at the grocery store which has been hit the hardest of all retail stores by the chain plan, and all chains are alike—grocery, drug, cigar or what-not. Can you picture the old grocery store? The flies had a picnic in the sugar barrel; the mice played golf in the rice barrel, and the cats slept on the spinach. The store was sticky and dirty from the drippings of the molasses barrel. Modern people demanded something different. So the chain store stepped in and put in a clean store and the mice hunted another golf course and the flies another picnic ground and the public were pleased, and the chain grocery store, because the independent grocery man had lost an opportunity to sense what the public wanted and demanded, flourished

Take the chain cigar stores. Before the Chain Cigar Stores came into existence, 90 per cent of the cigars, cigarettes and tobaccos were bought in drug stores and about 10 per cent in the old-fashioned tobacco stores. What happened when you and I went into a drug store to get a cigar? We first had to make a loud noise to let the proprietor know we wanted to buy a cigar. Usually we rapped our nickel on the counter. Then he came to us and waited on us. What did we get? We got the cigar that we asked for in a bad, damaged condition, dry as powder and without flavor because it had been kept improperly and had been neglected. The Chain Cigar Stores capitalized on just those two things—prompt, careful, polite and quick attention to the customer and the cigars in the condition that they should be and they built their business on that. All just because the retail druggist neglected to take account of what the public wanted and demanded.

Then came the chain drug stores, and the chain drug store, without talking about price cutting, without talking about advertising to attract the public, set up

a drug store that was clean; the merchandise was arranged attractively, the windows were polished, the lighting was done scientifically and the clerks were polite and quick to wait on those who came in. Those are the fundamentals of the chain drug store, and it grew because the independent druggist of other days had not seen the trend of the times. His ear had not been down to the ground.

What does Dr. Copeland of the Harvard Bureau of Business Research say? Let me read you just a line of what he says:

"The fact that so few units, individual stores, have materially improved their methods of management and operation points to one of the major reasons for the continued chain store growth."

He is a disinterested observer, a scientific observer, if you please, without prejudice. He is not speaking of just drug stores but of all the chains.

While I am on that subject, quoting outside criticism, which is the helpful criticism, in the *World's Work* not more than six or eight months ago there appeared an editorial on chain stores. These editorials are written by men especially equipped to write editorials; they are hired and employed for that purpose; they are keen observers and able to write the things they see. The writer, after going over the growth of chain stores, sums up his entire survey and remarks on chain stores with this paragraph:

"It is fitting that the growth of chains should be challenged and analyzed, but there is little likelihood that the development of more soundly managed chain systems will be retarded. What is certain is that under the new regime only those independent merchants who can keep up to the new standards of efficiency and competency will survive."

And that is as true as God made little apples. Only as you can keep up to the standards of efficiency and competency will you survive.

Without holding any brief for chain stores, either for or against them, I say to you gentlemen in the retail business, the chain store is the last word in efficiency in merchandising and good storekeeping. And good storekeeping covers it all. Good storekeeping, good housekeeping—walk into a home—the instant you step over the threshold you know whether the housewife is a good housekeeper. Walk into a drug store and you immediately know whether he is a good storekeeper. Copy the methods of the chain store in storekeeping and you will go a long way toward correcting—the diminishing of total sales and net profits.

The independent retail druggist is in a more preferential position to combat the chain store than any merchant in any other line is to combat the chain in his line. Chain stores are impersonal. They are simply machines. There isn't any personal contact. The public of this country in their drug dealing want personal contact; they want personality and they are going to eventually demand it. So if we druggists will capitalize that one thing, that priceless ingredient to quote one of our contemporaries—of their personality and individuality—plus their professional training, and then take note of the present trend of merchandising, (not prices—you have got to make your prices conform with the accepted level), he can and will succeed in conducting a profitable business.

Twenty-five years ago locomotor ataxia was a disease; to-day it is a dance. Things are going faster. You have to take that into consideration. What can be done? What is there available? There is the machinery available to preserve,

maintain the independent retail druggist in business profitably. He is a necessity. You don't doubt that; I don't think you will dispute that with me. He is as great a necessity as the water supply of this town is a necessity to its citizens. I wager that the people of this town are alert and keen to see that their water supply is not contaminated or lessened. So we, as the leaders in pharmacy, must see to it that the service that is necessary is rendered properly and in a manner that is acceptable and helpful to the public.

We have the personality of the individual druggist in his contact with the public, and its confidence and respect has not yet been dissipated. They still have it; they still believe in the pharmacist. He stands equally in the public's respect and confidence with the professions of medicine, law and theology. They still look up to him as a professional man, a man in whom they can place their confidence, and you have got to safeguard that by letting the public know just how you stand and how you feel toward your business. With these fundamentals, with a lower cost of doing business than the chain stores, lower expense figures by at least 2 to $2^1/_2$ per cent, you have that edge on the chain store, but you have got to be *good* storekeepers. Every drug store is equipped with scales, balances, spatulas, bottles, corks, labels, all the way down to cigars and the soda fountain. I wonder if they are equipped with two of the most important pieces of apparatus, namely, the dust cloth and the mop. They often look like they are absent. If you haven't got them, get them and put them to work.

In your city, every druggist's city, there is a professional engineer on illumination. Consult him. Have your windows and stores lighted right. Sell those things that are normally found in the drug store and that the public expect to find there. The public smiles when it sees coffee pots on sale in a drug store, it doesn't enhance their respect for the druggist. I don't have to go into those things. Accept those things that are so obvious and apply them to your business. The independent retail druggist is an integral part of the social make-up of our country. He is a necessity, a national necessity, and it is up to us to be willing to accept those things that are beneficial, that are helpful and that are being used and constructed for our benefit. Nothing can be done without you making the effort to help yourself.

Pharmacy Week is a wonderful thing—a propaganda carrying to the people some idea of what the drug store is and what it does. There is where we have been lax. We have not blown our trumpet as we should. Medicine has never hesitated to blow its trumpet. Medicine has never hesitated to let the public know of its efficiency and necessity. Let us as pharmacists carry on a propaganda teaching the public what pharmacy is and what it stands for. Pharmacy is being accepted more as a necessary profession than ever before, but it is up to us to persistently inform the public about Pharmacy and its importance to the Public Health—for Pharmacy is the foundation stone of the Drug Store and the Drug Store is a National Necessity.

ABSTRACT OF PAPER, SCIENTIC SECTION.

"The Mercuration of Phthaleins in Neutral Solution with Bichloride of Mercury," by Frederick R. Greenbaum.

Series of mono- and di-mercury compounds made when neutral solution of sodium salts of phthaleins act with boiling concentrated solution mercuric chloride.

DEPARTMENT OF BUSINESS MANAGEMENT

Conducted by Paul C. Olsen.*

COMMENTS, QUESTIONS AND SUGGESTIONS ARE INVITED AND WELCOME.

Readers are invited to submit comments, criticisms and suggestions regarding the material which appears in this department. The Editor also will undertake to answer questions regarding general problems of business management. Letters of general interest will be published, but the writer's name will not be revealed without his permission.

POPULARIZING THE PREPARATIONS OF THE UNITED STATES PHARMACOPŒIA AND NATIONAL FORMULARY.

(*Continued from p. 1027.*)

Many are the doleful predictions about the future of pharmacy. It is a favorite subject of the cartoonists and vaudeville actors, and the old jokes about being able to buy everything but drugs in a modern drug store are being revamped in accordance with recent trends of the times.

With these frequently-made comments in mind, the suggestion that it is possible to create a wider use of the preparations of the United States Pharmacopœia and National Formulary is likely to be considered by some, an impossible one.

Pharmacy Week has come and gone. More Pharmacy Week window displays were used in the United States and other countries than ever before. More publicity in more different media, including the radio, was given to Pharmacy Week than ever before. Pharmacy Week windows were not only more numerous but attracted more attention than ever before. The world map showing the sources of the principal drugs listed in the United States Pharmacopœia and National Formulary, which was distributed to retail druggists by the members of the National Wholesale Druggists' Association, attracted attention wherever it was displayed. This was especially true when displays of the drugs themselves, sources of which were shown on the map, were also displayed with the map.

Doesn't this world-wide and rapidly increasing interest in professional pharmacy, both within and without the drug trade, indicate that, in spite of the luncheonette and other drug store side-lines, the professional aspects of pharmacy are of consuming interest to the general public, if only those engaged in the drug trade will take the trouble to bring them before the people?

Pharmacy Week is intended not as a means of promoting the sales of specific merchandise, but to increase public interest in professional pharmacy. With the interest which it has been demonstrated can be created by such an event as Pharmacy Week, it certainly appears evident that a retail pharmacist, if he will, can use this interest to promote the sale of products which are representative of the professional side of pharmacy.

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This is an easy statement to make, but a far more difficult one to carry out. I think that nearly all druggists will admit that they probably can increase the sales of U. S. P. and N. F. preparations, but where to begin?

A general campaign to increase interest in U. S. P. and N. F. preparations is likely to produce general results—that is, no definitely measurable increases in sales of such products are likely to occur.

How can they, because, with hundreds of preparations listed, it is a physical impossibility to bring them all before the professional and lay patrons of a pharmacist in a general campaign. If he can't do this, how can he expect these people to make their own selections from the many pages of these two standards?

There is an additional practical difficulty, in that part of the preparations of the U. S. P. and N. F. are regularly dispensed—in fact, must be or should be dispensed, only on physicians' orders.

On the other hand, there is another group of preparations which, as I mentioned in the preceding article in this series, are commonly accepted household remedies which physicians actually encourage people to buy from their druggists. The surprising thing, as I suggested in that article, is that so few of them, necessary and desirable as they are, are to be found in the medicine chests of even the best informed families.

The following list of household remedies taken from the U. S. P. and N. F. is not complete. It is simply included here for purposes of illustration to show definitely a few of the specific items of merchandise to which a druggist may find it profitable to give serious attention in promoting their sale, instead of preparations, the components of which he is not informed about.

Spices, cream of tartar, tartaric acid, citric acid, boric acid, alum, sodium bicarbonate, sodium borate, magnesium carbonate, calcium carbonate, cochineal and other colors, flavoring essences; glycerite of starch, lactose, perfumed spirit, benzoated suet, hamamelis water, aromatic vinegar, dentrifrice, mouth wash, alkaline aromatic solution, compound solution of cresol, solution of chlorinated soda, tincture of green soap, glycerin; spirit of peppermint, spirit of camphor, hydrogen peroxide, cataplasma kaolin, paraffin dressing, petroleum jelly, carron oil, tincture iodine, tincture of arnica, cold cream, collodions, potassium nitrate papers, aromatic spirit of ammonia, ammonia liniment, oxide of zinc ointment, Epsom salt, solution of soda and mint, solution of calcium hydroxide, compound resin cerate, camphorated brown plaster, soap plaster, soap liniment, chloroform liniment, camphorated oil, acetic turpentine liniment; aromatic castor oil, emulsion of castor oil, oil of wintergreen, liquid petrolatum, cod liver oil, cod liver oil emulsion, Rochelle salt, seidlitz powders, effervescing salts, milk of magnesia, glycerin suppositories, honey of sodium borate, compound powder of glycyrrhiza. With even this incomplete list before him, it is evidently possible for a druggist to determine for himself the selling possibilities of the preparations mentioned and others listed.

Some druggists will say they have no sale whatsoever for some of the items listed, and for others they will say there are proprietaries which are more suitable or at least which are in greater demand. I have no quarrel with such statements; it is only natural that the demand for preparations of this kind—in fact for products of any kind—should vary with localities and inclination of proprietors.

The five basic factors which determine the salability of the product are listed below. With these five basic factors in mind, I think it is possible and practical for any druggist to take each of the items of the list and determine whether they deserve selling effort on his part. That is not the end of the story, however. Merchandising is far from an exact science and the only way to prove the salability of a product, even after such an analysis, as suggested, is by careful test and try-outs in the store: Window displays, counter displays, store detail, and detailing doctors, dentists and others requiring such preparations.

The first of the five factors which determine the salability of a product is its uses. What are they and are they uses which will appeal to the patrons of the store? Cold cream, for instance, is a larger proportion of the sales in some stores than it is in others. This may be due to merely a lack of selling effort or it may be due to the characteristics or occupations of the people this store serves.

The second factor is the determining of the salability of the products as to its users. Who are they? How many are they? And are they all going to be interested in the preparation? Obviously, if only a small proportion of a store's patrons can be interested in a product, selling effort can be expended more profitably on some item with a wider appeal.

The third factor is sales frequency—that is, the rapidity with which the item is used and bought again. An item such as soap liniment may sell to a rather large number of people, but it is used so slowly that repeat business is likely to be very slow in coming. The same thing is true of tincture of iodine. On the other hand, such products as cod liver oil, Epsom salt, boric acid and cold cream are used rapidly and the opportunity for quick repeat business is much greater.

The fourth factor is competition. How much competition is there? How aggressive is it? Some preparations of the U. S. P. and N. F. have little or no competition from similar proprietaries or from other U. S. P. or N. F. preparations. A product in which there is little or no competition involves, many times, the necessity of educating its prospective patrons to its desirability. On the other hand, a product which has many competitors finds ready acceptance, but an individual druggist has his difficulties in obtaining his share of the business.

The fifth factor is the selling and distribution methods used. For instance a druggist, to-day, would have more difficulty in obtaining business in spices and flavoring extracts than he would have had years ago when the drug store was almost the only outlet for merchandise of this type; now almost all the business goes through the grocery trade. The very fact that many of the household remedies listed in the U. S. P. and N. F. can be sold only by licensed pharmacists is a decided advantage to the druggist who is trying to promote the sale of these preparations. He has little or no legal competition from other types of stores.

(To be continued)

No single group in pharmaceutical activities can stand alone, and is helpless in a degree, without the support and coöperation of the other associated and related groups.

CLINICAL LABORATORY WORK A PRESCRIPTION AID.*

BY LEE S. COY.[1]

Many qualified pharmacists, no doubt, have overlooked the possibilities of clinical laboratory work as a means for increasing their prescription business. Several papers could be presented on the subject of clinical laboratory work; as, for instance, "Increasing Biological Sales with the Microscope," "Combating Cut-Rate Stores with Professional Assets" and "Clinical Laboratories a Source of Income to the Pharmacist." However, in this brief paper I wish to bring out some of the possibilities of clinical laboratory work as an aid to the Prescription Department.

Our business was established about ten years ago as an upstairs Prescription Shop and branch of the State Board of Health laboratory. We do all types of laboratory work, such as blood counts, blood chemistry, Kahn test, bacteriological cultures, fecal analysis, protein tests, milk analysis, dark field examinations, urine analysis.

Blood and urine, of course, are the larger fields for laboratory tests and are, perhaps, the best sources from which we receive prescriptions, as a result of our laboratory tests. In a great many cases our laboratory reports are telephoned to the doctor and a written report mailed later. Quite frequently a prescription is dictated to us during our telephone report to the doctor, who directs his patient to come to our shop to get the prescription. By the use of phone reports of our laboratory findings, we are also given the opportunity of suggesting new prescription items and to make sales of physicians' supplies which otherwise we might not make.

A few weeks ago we received a call from a local doctor to come to the home of one of his patients and make a blood count and differential slide. The call was made promptly and within the hour our laboratory findings were telephoned to the doctor. The patient had a very low erythrocyte count and the differential slide showed a typical picture of Pernicious Anemia. In the course of the conversation the doctor asked that we send to his office a package of ampuls of Iron Arsenite and Strychnine, remarking, "that he would treat the patient with them, although he expected her to die in a few weeks." We suggested liver therapy to him and after a little explanation of its use in such cases, he prescribed an eight-ounce bottle of Liver Extract. The patient began improving and we have refilled the prescription quite regularly since the original prescription was given us. This is a splendid case illustrating the value of clinical laboratory tests as a factor in increasing prescription sales. In this case we were able to convert a 25 per cent pharmaceutical sale into a profitable prescription sale with steady repeat business. In such cases as Pernicious Anemia the original blood count is not the last we see of the patients, as they require frequent check-ups of their erythrocyte count. Here again, our Prescription Department profits, as the mode of administration is often changed to meet the whim of the patient, Liver Extract in capsules, vials and liquid form together with dilute solutions of hydrochloric acid, Acidulin and similar products being prescribed.

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* Section on Practical Pharmacy and Dispensing, A. PH. A., Rapid City meeting, 1929.

[1] Security Laboratories, Cedar Rapids, Iowa.

Not all blood counts, of course, show Pernicious Anemia, as we find that secondary anemias are by far in the majority. Conditions of this type result from many causes and we leave it strictly up to the doctor to find the cause. It is, however, a very good field for prescriptions and we receive a great many for such items as Elixir Iron, Quinine and Strychnine, N. F., Compound Syrup of Hypophosphites, N. F., Compound Elixir of Glycerophosphates, N. F., Metatone, Spleenmarrow liquid and capsules, and cod liver oil, in all its forms. In anemic cases, due to hemorrhage, prescriptions for Thromboplastin, Hemostatic Serum, Normal Horse Serum, Fibrogen and combinations of gland products such as dessicated Ovarian, Corpus Luteum and Thyroid Extract are received.

Occasionally we find an erythrocyte count of seven or eight million and in such cases prescriptions for Phenylhydrazine hydrochloride are received. Cases of this kind require frequent blood counts in order to control the destruction of the erythrocytes and refills of prescriptions are quite regular.

Frequently the leukocyte count runs quite high, as in many acute cases, and we are able to obtain many prescriptions for Codeine, Amytal, Cibalgine, Allonal, Ipral and Neonal.

A great many of these cases go to the hospital for operations and through our contact made while doing clinical tests we are also able to send out sick room supplies, such as hot water bottles, ice bags, enamel ware and rubber sheeting.

Blood sugars are very important sources of information in treating diabetes. We do several such tests each week and numerous prescriptions are received for insulin, hypodermic syringes, hypodermic needles, Benedict's solution and dietetic foods from this type of clinical tests. Time will not allow a discussion of all the various blood tests from which the Prescription Department benefits, but a word should be said about Kahn tests for syphilis. In positive cases of this kind many prescriptions for the arsenicals, mercurials, bismuths and iodides are received by the pharmacist and they are all very profitable to the Prescription Department. A great many pharmacists have not posted themselves in this important field. The man who can do the laboratory tests will find the way open to him to make many profitable sales. Here again the telephone report allows the pharmacist to suggest lines of arsenicals and other supplies of highest therapeutic value and to steer clear of those for which the manufacturer allows only a short margin of profit or of questionable therapeutic value.

The microscope discloses a great many scenes which require the services of our Prescription Department. Every morning a number of throat cultures are examined. Nearly all of them require prescriptions such as Liquor Antisepticus, N. F., or some of the new antiseptics, such as Solution Hexylresorcinol, Metaphen and Acriflavin. Stock solutions are also supplied to the doctors, such as Mercurochrome solutions, solutions of Silver Nitrate and Tincture of Ferric Chloride in Glycerin. Once in a while we find Diphtheria bacilli and orders are received very promptly for Diphtheria anti-toxin in such cases. Our Laboratory reports naturally are very good salesmen in such cases.

Too much cannot be said about the value of the microscope and a knowledge of Bacteriology in paving the way for biological sales. Every day we have telephone calls, both local and long distance, from doctors asking for information about the use of some biological product. Due to our laboratory service they

expect us to know what to suggest, and we try to keep posted through contact with the detail man and the medical literature. Our sales in biologicals run up to several hundred dollars a month as a result.

Vincent's Angina has been very prevalent lately and we have developed a very nice prescription business on a mouth wash of our own manufacture. When we examine smears from the gums or throat and find Vincent's organisms present we always make it a point to call the physicians' or dentists' attention to our preparation. Prescriptions at the rate of ten or fifteen a day are the result.

The whirl of the centrifuge in urine analysis bringing down sediment for examination under the microscope is another good field for prescriptions. Here the report of pus cells, blood cells, casts, bacteria and the result of chemical tests suggest many prescriptions to the doctor. Pyridium, Hexamethylamine Tetramine, Caprokol, Oil of Santalwood, Van Cott's Vaccine and F. E. Buchu, U. S. P. and many other preparations receive their call.

Summing up, clinical laboratory work:

(1) Helps us maintain a professional status. (2) Gives us close contact with the doctor and patient. (3) Increases our biological sales. (4) Allows us to suggest profitable pharmaceuticals. (5) Eliminates the merchandising of patent medicines and sundries. (6) Lowers overhead. (7) Laboratory fees are an important source of income. (8) And last but not least, gives us the opportunity to practice ethical pharmacy.

Truly we have come to believe that our microscope is as important as our mortar and pestle in maintaining our Prescription Shop.

ABSTRACT OF DISCUSSION.

W. H. Glover inquired what discount was given on biologicals. The author replied that the physicians receive 25% from list, others pay list price. He referred to a number of items and the profit to be derived.

E. Fullerton Cook classed the paper among the best ever presented before this Section; he inquired relative to the population of Cedar Rapids. Prof. Cook stated that the paper points the way to future pharmacy. He referred to a pharmacy in Wilmington, Del., and said that it takes men who are scientifically trained, who have the professional vision to conduct a professional pharmacy. He also made reference to a pharmacy in New York, wherein three people do the laboratory work. These pharmacists have a pharmacy in the Professional Building and have been invited to open a professional pharmacy in the Medical Center in New York City.

Prof. Cook spoke of the terms "ethical," "commercial" and "professional;" he said a commercial store could be ethical and a professional might be unethical. He is desirous of having the term "professional pharmacist" rightly applied. In his opinion there is a real and growing opportunity for the practice of professional pharmacy, because of higher educational requirements and more extended training.

William J. Husa referred to the location of the laboratory under discussion in the paper; at the beginning the prescription business was not encouraging, but it developed in a city and section where physicians dispense their own prescriptions. In this city is a small manufacturing house, catering to the dispensing physician. They supplied the physicians with preparations dispensed by them and with bottles, corks and labels for the prescriptions.

A. O. Miçkelsen said that in some states the laboratory work is directed to be done by doctors of medicine. In his opinion qualified pharmacists for such work would be welcomed by physicians. He had visited a pharmacy in Denver where ampuls of special formula were prepared for physicians' practice; he asked why they did not take up biochemical work and the reply he received was, that it would be trespassing on the rights of physicians. He was glad that some pharmacists were making a success of this work.

William Gray regretted that such work was not more generally carried on by pharmacists.

Mr. Coy said that in his section it was a common practice for physicians and hospitals to employ so-called Laboratory technicians, graduates of 6-week training school, to do laboratory work. He cited the case of a former instructor of pathology in a large University school of medicine now in private practice who employed technicians with little training to do his routine work at a hospital where he had the contract to do the work. Some day a serious error will result, because the assistants have not the necessary background and training.

E. Fullerton Cook said he knew of a number of pharmacists who were employed in laboratories of physicians.

A. O. Mickelsen remarked that this kind of work should be done by trained pharmacists. On his vacation trip he called on a doctor who was making hay fever tests and had the opportunity of giving him assistance by correcting his method. In his opinion doctors will gladly coöperate with pharmacists in this kind of work.

Clyde M. Snow referred to a graduate in pharmacy of about fifteen years ago, who engaged in laboratory work and secured the active coöperation of the physicians in Joliet, and succeeded. In his opinion, physicians who understand the work, and can do it, are glad to have pharmacists, who are qualified, take over this practice; physicians have high regard for qualified professional pharmacists.

THE PRESIDENT'S ADDRESS OF THE BALTIMORE MEETING IN 1898.

Henry M. Whitney, of Boston, presided at the Baltimore meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1898. A few lines from the closing paragraphs of his address follows:

"As sure as the sun rises in the East and gives us light, as sure as the North Star has been a guide to the mariner, so sure is it that the AMERICAN PHARMACEUTICAL ASSOCIATION has been and will continue to be the light and guiding star of the coming pharmacist. Because clouds sometimes obscure the light, or storms and contentions drive us from our course, are we like the clam to bury ourselves in the sand? There is a future for pharmacy; there is work for us to do at the present, and in the future as in the past. * * * I repeat there is a future for pharmacy; and the future may be likened to the mining industry. Mines that have been profitably worked and exhausted, as supposed, have under modern skill and science been re-opened and worked more profitably than before. So pharmacy to-day in a few places is testing and experimenting on the lines of assay, analysis, microscopy and bacteriology.

"As we of the past and present pass off the stage, the future will be nearer and nearer the ideal, and we of the past, as in the painting by Malbone, may linger for a moment while the light of the present falls upon us.

"I feel like crying aloud, 'Good Lord, deliver us from the pessimist; stir up the optimist; and as by Thy help we have made long strides and accomplished much upon the educational side, so guide and direct us in our efforts of good stewardship on the commercial side, that we may be prepared for the welcome—well done, good and faithful servants.' "

THE RED CROSS AND THE CHRISTMAS SEALS.

The period of the annual roll-call is now on and extends to Thanksgiving Day. Pharmacists are always interested in this work and have the opportunity of giving publicity to this, one of the greatest services rendered to humanity. The Red Cross has a part in relieving the suffering and loss incurred by cyclones and other storms, fires, floods, wrecks and epidemics. The standard of the Red Cross is a sign of hope in the midst of confusion and sorrow; it is an organization which asks no questions as to race, creed, politics or color; its purpose is in a service which requires and should have the coöperation of every one. As stated, pharmacists will not only do their bit but carry the message to others. The purpose of the Christmas Seals, and support of the Crippled Children's Hospitals, in the service of which no questions are asked relative to creed or race, also deserve a related tribute and encouragement.

Readers will be interested in the succeeding article on the development of professional pharmacies.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

C. B. JORDAN—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

PROFESSIONAL PHARMACY.

AN ADDRESS BY DEAN C. B. JORDAN, DELIVERED AS A PART OF THE PROGRAM OF THE SECOND GENERAL SESSION, A. PH. A., RAPID CITY MEETING, 1929.

I believe there is growing up a gradual separation of commercial and professional pharmacy, especially in the large cities. This movement is not revolutionary but evolutionary and will take a great number of years for completion, if separation is ever fully accomplished. I have watched this movement with a great deal of interest and believe that its speed is accelerated by the advent of the chain store and the development of commercialism in all lines of retailing.

More attention is given to the science of retailing to-day than ever before in the history of this country. The old-fashioned merchant, who opened a store, displayed his merchandise and sat down to wait for customers, has gone and a new energetic "go-getter" has taken his place. Advertising, business economics, salesmanship, overhead, leaks, etc., have all been carefully studied and the average druggist is rapidly becoming an expert business man. The old-fashioned shelf bottles have been relegated to the back room and the store has taken on the appearance of a sales counter with everything price-tagged. It is but natural that such changes would hurry a separation between commercial and professional pharmacy. Whether or not we are in favor of such a separation and whether or not it is for the best interest of pharmacy in all its phases, we should, in my opinion, study this movement and endeavor to see where it is leading us.

This movement will be very slow in reaching the smaller cities and, perhaps, will never come to towns less than 10,000 in population. In the cities, however, it has gained rapid headway during the past decade. In a recent visit to the City of St. Louis, I found four professional pharmacies and three highly developed commercial drug stores within the radius of two blocks. Two of these commercial stores belong to chains and one of the professional pharmacies was over a chain store. The interesting fact is that, apparently, there is no competition between the two types of pharmacies. I suppose this condition is duplicated in many of our larger cities.

I wrote the following letter to a number of professional pharmacies—to determine the extent and success of the separation:

> DEAR SIR:
>
> I am very much interested in securing information regarding the development of professional pharmacy. I believe there is a decided trend toward the *gradual* separation of commercial and professional pharmacy. If I can secure sufficient information, I hope to present a paper before the AMERICAN PHARMACEUTICAL ASSOCIATION on this subject.
>
> A professional drug store, as I mean it, is one that emphasizes the compounding of prescriptions and carries only those side lines that supply the medical needs of

the home, that is sick room supplies, mouth washes, dentifrices, etc., and carries no proprietary medicine except those that physicians tell their patients to buy, such as milk of magnesia, mineral oil, etc.

I understand you are conducting a professional drug store and I will appreciate it if you will give me the following:

1. A picture of the store from which a slide can be made, if you have such.
2. The date the store was opened as a professional pharmacy.
3. The number of registered pharmacists employed.
4. Number of prescriptions compounded per year.

I fully appreciate that this latter information is private and I certainly will not give it in connection with any store, but I would say that store No. blank compounded blank No. of prescriptions per year.

Any assistance you can give me in developing this subject will be greatly appreciated.

Sincerely yours,

C. B. JORDAN.

Many of the proprietors were very kind and answered my letter fully, others were too busy to secure the extra data and probably threw the letter in the waste basket with the comment, "Another one of those fact-finding cranks." In a conversation with President J. K. Lilly, of Eli Lilly and Co., I told him what I was endeavoring to do. He showed interest in the subject and offered to secure information for me through the representatives of his company. Accordingly, I submitted to him a list of cities that my letters had not covered and he secured the information I desired. I am sure that this report is not complete and probably we never will be able to secure a complete report of professional pharmacies. It is a start, and will show the trend of separation.

I secured the names and addresses of the professional stores by calling upon my friends, located in cities, for this information. All that I called upon very graciously gave me assistance and my thanks are due to them. I sent out over 100 letters and received 40 replies, so my batting average is about 40%. Mr. Lilly, through personal visits by his representatives, secured 90 reports, so his batting average compares favorable with Babe Ruth's. These reports came from all parts of the United States, from Boston to San Francisco and from Minneapolis to New Orleans. I doubt if any city of 50,000 has been overlooked. It is interesting to note that the spread of professional pharmacy is effected by local conditions. In some large cities there are no professional stores, while in others there are a great many.

I found it very difficult to define a professional pharmacy in such terms as permit of sharp classification of all drug stores. Many drug stores make a special feature of their prescriptions and are doing a splendid professional business but, at the same time, are carrying the usual stock of the drug store. The question arises "Should such stores be classified as professional drug stores?" I found considerable difficulty in answering this question and, finally, avoided it by including all that reported to me. However, I am sure that the number of not strictly professional stores that reported is not more than 5 per cent of the total and I believe we can consider this insignificant.

The question of how to get this data before you troubled me a great deal until a photographer friend suggested that I have a stenographer copy it and he would

photograph it and make slides for me. I hope that all will be able to read the slides. The stores are not arranged in any order so it will be impossible for any one to identify any report unless there be present some proprietors who recognize the figures they sent in.

Three facts are reported for each store: A, Date of establishment; B, No. of registered pharmacists employed; C, number of prescriptions compounded annually.

Store no.	Date of opening.	Prescriptionists.	Annual no. of prescriptions.	Store no.	Date of opening.	Prescriptionists.	Annual no. of prescriptions.
1	1927	2	15,000	48	1923	2	2,700
2	1926	2	9,000	49	1820	12	82,000
3	1928	2	10,000	50	1914	3	12,000
4	1906	3	22,000	51	1928	3	20,000
5	1899	3	15,000	52	1906	4	60,000
6	1905	1	12,000	53	1925	3	15,607
7	1870	4	25,000	54	1895	16	81,433
8	1928	1	11,000	55	1929	2	25 daily
9	1928	2	6,000	56	1918	2	No answer
10	1900	2	40,000	57	1920	2	12,432
11	1925	3	28,080	58	1888	3	?
12	1904	4	46,815	59	1896	10	84,000
13	1909	3	28,000	60	1923	3	50,000
14	1881	3	30,115	61	1927	3	65,000
15	1872	4	36,500	62	1924	2	4,500 est.
16	1923	3	18,350	63	1929	2	4,500 est.
17	1926	2	9,500	64	1928	2	2,000
18	1922	2	10,500	65	1881	4	24,850
19	1929	1	3,500	66	1918	1	3,000
20	1899	6	60,000	67	1916	3	6,000
21	1900	3	25,000	68	1920	3	15,000 est.
22	1926	3	9,500	69	1927	1	1,500
23	1890	3	10,000	70	1929	2	10 daily
24	1928	2	5,000	71	1928	2	12,500
25	1890	3	10,000	72	1927	3	12,000
26	1890	3	10,000	73	1926	1	6,000
27	1919	1	8,000	74	1923	3	20,000
28	1917	6	30,000	75	1914	6	68,000
29	1800	8	35,000	76	1925	2	25,200
30	1929	2	10,000	77	1910	6	40,000
31	1928	3	10,000	78	1927	6	70,000
32	1890	3	25,000	79	1926	2	20,000
33	1898	5	50,000	80	1903	7	75,000
34	1885	3	7,500	81	1921	4	30,000 est.
35	1926	4	20,000	82	1917	3	20,000
36	1921	5	27,000	83	1921	2	10,400
37	1929	3	18,000	84	1925	1	10,000
38	1927	2	24,000	85	1927	2	15,000
39	1923	2	28,000	86	1922	2	10,000
40	1923	3	50,000	87	1929	5	36,000 At present rate
41	1925	1	9,600				
42	1913	3	26,000	88	1924	4	40,000
43	1923	2	15,000	89	1923	3	28,000
44	1911	2	4,768	90	1917	4	38,000
45	1927	3	16,500	91	1908	4	36,000
46	1888	6	29,000	92	1925	6	35,000
47	1927	1	8,000	93	1925	4	46,600

Store no.	Date of opening.	Prescriptionists.	Annual no. of prescriptions.	Store no.	Date of opening.	Prescriptionists.	Annual no. of prescriptions.
94	1924	5	50,000	106	1913	13	63,000
95	1929	3	20,000 new location	107	1925	2	5,000
				108	1924	3	7,200
96	1912	2	22,000	109	1918	7	60 to 70,000
97	1869		2,000,000 to 6/26/29	110	1907	–	1,166,100 to date
98	1923	3	5,000	111	1912		3 stores doing
99	1929	3	20,000 at present				$200,000 a year
100	1870	2	6,500	112	1915	3	19,000
101	1927	2	7,000	113	1926	2	3,000
102	1912	5	45,000	114			13 in 3 stores 54,050
103	1902	2	160,000 to date	115	1899	10	45,000
104	1925	9	100,000	116	1926	2	21,900
105	1889	12	60,000	117	1904	9	1,286,000 to date

The foregoing list is far from complete as many replies gave me a great deal of information but not the data that I wished and, without doubt, a number of professional stores were not approached. I believe the information contained does show a decided trend on the part of American pharmacy to separate into two distinctive types, professional and commercial. I am convinced that this trend is only in its infancy. Of the 117 stores reported, 64 or 54.7 per cent were established in the last nine years and 44 or 37.6 per cent in the last five years. Eliminating 16 reports for which we have no accurate data, these stores are compounding an average of 16,300 prescriptions per year, or 45 daily. I feel sure that there are a goodly number of non-professional stores that equal or exceed this average. However, we must not lose sight of the fact that 54.7 per cent of these stores were established within the past nine years and it takes considerable time to build up a professional business.

I wish that time permitted me to give you all the interesting comments I received in answer to my letters. I will endeavor to pick out the most interesting ones. A number commented on the time it takes to build up a professional business and the discouragements that are met with. I can best illustrate this by quoting from a recent address before the Indiana Pharmaceutical Association by Dr. Leonard Seltzer of Detroit, who, we all know is conducting one of the most successful professional pharmacies in the United States, that he compounded an average of only three prescriptions a day during his first year in business.

Another states "The first two years, 1911 and 1912, were a complete failure. The expenses amounted to $11.00 per day and the income scarcely ran over $3.00 per day. Although my friends advised me to give it up, I stuck to it and simply made the best of it until I won out. Last year, 1928, we filled over 40,000 new prescriptions besides a great many repeats."

Another point frepuently stressed was location. The professional store must be located near a goodly number of physicians' offices or it is doomed to failure. One man commented as follows:

"There were in this building twenty or more physicians, some of whom did not prescribe. At the end of one year about half went to a new building. This left me to get many of my prescriptions from outside of the building and I believe my continuance in business is due to a previous reputation and acquaintance in the neighborhood. A year ago an exclusive prescription pharmacy was opened in a

down town location with expensive fixtures, youthful enthusiasm, but no following. After six months they closed out and the proprietor went back to work."

Another states, "In the past six years there have been three strictly prescription pharmacies opened—two failed outright, one is in a miserable condition now. The latter is in an office building formerly housing 60 doctors, but with the erection of the *bank* building here, nearly all of the doctors moved."

Moral: Move with them.

"The 'Prescription Shops' as they are called in *blank* city are all of the type of store that you are interested in and in my opinon they will have a growing importance in the future. The idea, as it has been worked out in *blank* city is economically sound for the following reasons:

1. They have low rentals and low overhead expense.
2. They appeal to the discriminating physician.
3. Their net profit is at least one-third of their volume.
4. The hours they are open for business are comparable with other business and not nearly as long as other drug stores."

"I am glad to see that men of your type are becoming interested in professional pharmacy. The old trend of pharmacy needs to be revamped and it is not at all a credit to the pharmaceutical profession that they have become the legalized saloon keepers of the country."

"We feel that it takes time to develop in the public a sense of security and ethical professionalism in their druggist. Any one can sell a tube of tooth paste but the average man feels more particular about who fills his prescriptions."

"My store is run as a professional pharmacy and is opened at 8:00 A.M., closed at 7:00 P.M. on week days, and Sundays opens at 9:00 A.M. and closes at 1:00 P.M."

"Our store is open day and night. This in itself has proved a very good feature as the physician, when called late at night, oftentimes can save himself quite a long trip by calling us and prescribing the medicine required."

Evidently there is not a perfect agreement regarding the hours that a professional store should operate.

The type of service that should be given by the professional pharmacist is emphasized in several comments. The following serve to illustrate it.

"We enjoy the confidence of the medical men and try hard to deserve it. Our employees list increased to 14, 6 fully registered pharmacists besides 8 other helpers. Most of my clerks have been with me from 5 to 11 years. I find it a good investment to be strict in discipline but treat the employees like your own and they will stand by you. We have had no break in our official family within the last four years."

"Another interesting feature of our store might be, last year we filled over one million Seidlitz Powders, as our records show."

"We do not recognize Chain Store competition. We give the closest attention to our trade and let the public decide who is the most competent pharmacist. It surely pays to run a first class Prescription Store without lunch and soda water with ice cream. Prescription work is a specialty which few persons understand."

"*Service* is the watch word and that combined with super prescription work and supplying *only the best* drugs obtainable are responsible for our business. We

do not consider price until the quality has been ascertained and it must be *quality*. Another much stressed subject is, give the patient what the Doctor prescribed. Do not give him another make which may be as good or cheaper, but give him what his prescription calls for and charge him for it.

"When a prescription is turned out, fill it just as accurately and as carefully as if it were for your own family and have the finished product as neat as a professional pharmacist should compound it."

"There is no question in my mind but that there must eventually be a separation between the two branches of pharmacy. I firmly believe that the increased standards of pharmacy—the increasing of the length of time in College of Pharmacy together with other restrictions—will eventually solve the problem of the druggist."

"Just as medicine had to get rid of its quacks—so, too, does pharmacy have to get rid of its quacks, the only difference being that pharmacy has more quacks to get rid of. How can you expect to have the public respect certain pharmacists when they do not respect themselves? If we want the public to respect us as they do lawyers or doctors or even garage men we must act accordingly.

"We carry out a policy that no matter how busy we are, if a child comes in and asks for a drink of water politely, he will always get it, but you let the child or adult come in and ask for same in a manner showing no respect for the druggist in charge, he will not get it. We respect them and we in turn command respect. We do not argue about prices of prescriptions—we charge a fair profit and consider it professional service rendered. We do not fill our prescriptions up to a price—we fill them first and then price them afterward. We do not cut the prices on prescriptions—we have in force a schedule of prices that are followed by the stores that have been successful. We do not follow those that have shown themselves failures."

These comments could be extended at length but I believe they will only tire you. I have been impressed with the number of replies that read as follows: "There are no strictly professional drug stores in this territory." The territories referred to include some cities with population of 100,000 to 500,000. Evidently there is still a great opportunity for the development of professional pharmacies and we may expect to see this movement grow for some time to come.

I reported that the average number of prescriptions per year is 16,300. The largest number reported in one year is 100,000 and the store was opened in 1925. A store opened in 1896 compounded 84,000 per year and one opened in 1920 reports 81,433 per year. In contrast to these figures, a store opened in 1928 reports 2000 per year, one opened in 1918 reports 3000 and one opened in 1926 reports 3000 per year. Evidently it takes time to become established as a prescription pharmacist.

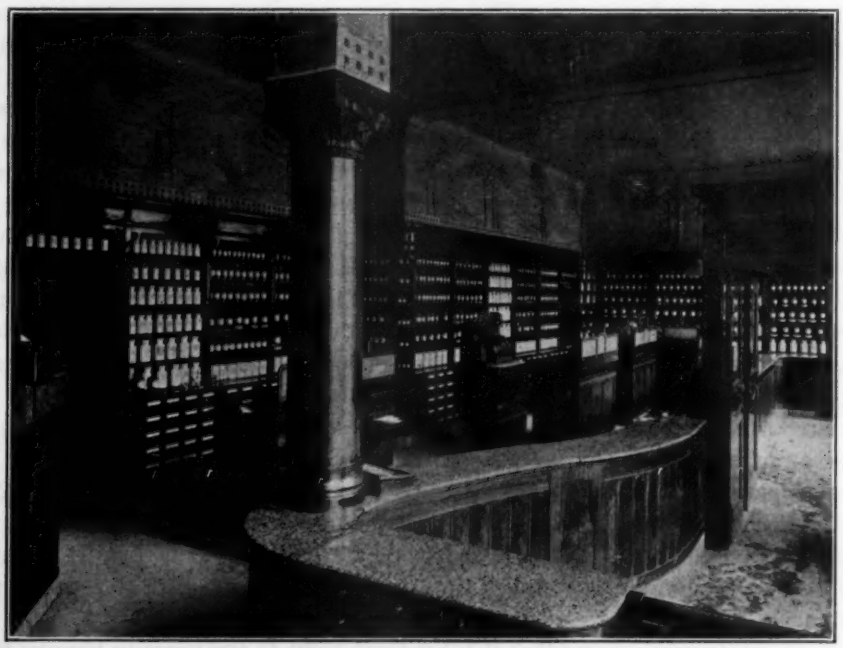
If we arbitrarily assume that it takes from eight to ten years to become firmly established in professional pharmacy and consider only those stores that were opened prior to 1920, we find an average of 35,000 prescriptions per year per store. In these same stores, one registered pharmacist was employed for every 20,300 yearly prescriptions. This makes practically 60 prescriptions per day for each registered pharmacist. Of course he may also have been employed in manufacturing and other duties about the store. This analysis could be continued, but when the figures are printed, each individual may analyze them as he sees fit.

I have prepared a slide showing some letter heads used by professional pharmacists, a slide showing a method of appealing to the public in favor of professional pharmacy and in opposition to commercial pharmacy and several slides showing professional stores. (These slides were shown by Dean Jordan.)

From this study I believe we are justified in stating that professional pharmacy is on the increase; that its development is only in its infancy and that we may expect a division of pharmacy in our larger cities into professional and commercial groups. It is my opinion that there will be little or no competition between these two divisions of pharmacy.

The study also emphasizes the importance of locating professional stores where the prescribing physicians are, and cultivating their acquaintance so that there will be close coöperation with them. It requires time, tact and patience to develop a professional business, but the reward justifies it.

If this movement continues, and there is no reason to believe it will not, I think there will be an opportunity to perfect a strong organization of professional pharmacists. Such an organization ought to be able to secure coöperation from the American Medical Association and thus build up an *esprit de corps* that will be mutually beneficial.



Knut Sjöberg Pharmacy, Stockholm.—Pharmacist Sjöberg was elected an honorary of the A. PH. A.—see page 896, September JOURNAL.

COURT RULES THAT PHARMACY IS A PROFESSION.

Mr. Justice Murphy of the British Columbia Supreme Court, on October 29th, in a case of the Provincial Minimum Wage Court, ruled that pharmacy is a profession.

THE DEPARTMENT OF THE NATIONAL ASSOCIATION OF BOARDS OF PHARMACY

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GENERAL NEWS.

Dr. E. V. Zoeller, for many years president of the North Carolina Board of Pharmacy, was elected honorary president of the AMERICAN PHARMACEUTICAL ASSOCIATION at the recent Rapid City meeting. The National Association of Boards of Pharmacy and the North Carolina Board deeply appreciate the honor conferred upon Dr. Zoeller, whom these two bodies claim as a member, and extend heartiest congratulations to him. Dr. Zoeller has been very active in the N. A. B. P., having served as vice-president and chairman of District 5 as well as being a member of a considerable number of committees.

The Columbus Retail Druggists' Association and the Ohio Pharmaceutical Association gave a dinner in honor of Dr. C. A. Dye, dean of the College of Pharmacy of Ohio State University, as a part of the National Pharmacy week celebration. President Charles Ehlers of Cincinnati, of the Board of Pharmacy, spoke on "Board of Pharmacy Examinations," and President J. S. Rutledge, of the Ohio Pharmaceutical Association as well as member of the Ohio Board, was also one of the speakers of the evening.

H. H. HOFFMAN, 1871–1929.

H. H. Hoffman, for many years Director of Drugs and Drug Stores for the State of Michigan and a member of the Board of Pharmacy, passed away on October 7, 1929. About two years ago, he had resigned these positions, owing to ill health.

In an autobiography filed in the N. A. B. P. office, Mr. Hoffman stated that he passed pharmacy board examinations in ten states and finally located in Sandusky, Michigan, after eight years of "seeing the U. S. first." He was prominent in Michigan and held a number of public offices—serving as a member of the state legislature and also county food administrator during the World War. He was appointed to the Board of Pharmacy by Governor A. E. Sleeper in February 1917, and also served as its president. In 1920, he was a member of the U. S. Pharmacopœial Revision Convention which met in Washington, D. C.

Michigan has lost one of its leaders in pharmacy and the N. A. B. P. mourns the loss of one of its former very active and loyal supporters.

President F. W. Ritter, of the Arizona Board, is another one of the N. A. B. P.'s sportsmen. He spent two weeks, in October, in the wilds of the White Mountains of Arizona hunting deer and bear. Success unknown.

Herbert M. Lerou of Connecticut, ex-president of the N. A. B. P., and secretary of the Connecticut Board, was recently elected to receive the honorary 33rd degree in the Masonic order, which will be fully conferred on him at the next annual conclave in Boston. This is the highest honor bestowed by the order, and we take great pleasure in congratulating Ex-President Lerou.

Secretary Winne of the Virginia Board drove his family to Yellowstone Park after the Rapid City convention and reports a fine trip until the homeward journey. The experience of being caught in a snowstorm in summer was interesting, but fighting "gumbo" roads for a week to get back to the pavement was not much fun, especially when the rate of travel was fifty miles per day.

STATE BOARD NEWS.

Arizona.—An examination was held in Phoenix, November 13th, 14th and 16th, during State Fair week. Results will be announced later.

Many licentiates from other states are coming in by reciprocity to share in Arizona's prosperity. All are being placed, and the secretary of the board writes that more are needed.

Indiana.—William A. Oren, for some time past the inspector for the Indiana Board of Pharmacy, resigned on October 1st. Mr. Oren is well known in pharmacy circles, having served as president of the N. A. R. D. two years ago. Paul E. Wolter of South Bend has been employed by the board to succeed Mr. Oren.

Reciprocal registration has recently been granted to Mat J. Kolb, of Arkansas; LeRoy C. Beckert and Edward L. Shinkle, of Illinois; George R. Orme, of Tennessee.

Kentucky.—At the examination meeting held in Franklin on October 8th, seven out of a class of eleven were successful in obtaining licenses as registered pharmacists and five out of six were granted assistant certificates. William G. Hanschmidt, of Ohio was granted reciprocal registration.

The annual meeting of the Board followed the examination and the following officers were elected to take office January 1st: *President*, Linwood A. Brown; *Secretary*, J. W. Gayle; *Treasurer*, George Wilhelmi; *Chairman Executive Committee*, George D. Duncan. The Governor not having appointed the new member, the personnel of the Board remains the same for the present. The next meeting of the Board will be held in Covington, January 14th.

Maine.—Thirteen candidates were examined at the August meeting and two received licenses; fifteen were examined at the October meeting and seven were successful.

The state pharmaceutical association will meet in Lewiston on February 13th for its mid-winter meeting; the annual meeting is to be held in Rangeley, June 25th to 27th. Plans are being made for the revision of the pharmacy law and an attempt will be made to remedy some of the present weak spots.

Michigan.—The results of the August examination have just been announced, and 39 out of 158 taking this examination were successful.

Missouri.—As a result of the September examination, 36 registered pharmacist licenses and 13 assistant pharmacist licenses have been issued. The next meeting will be held in January at Jefferson City.

Reciprocal registration was granted during October to William H. Davis, of Georgia; Morgan R. Hohmann, of Iowa; Leslie A. Meyer, of Oklahoma; Ridgely C. Bennett, of Tennessee; and Harry F. Shindler, of Texas.

Nevada.—An examination meeting was held at Reno on November 12th. Reports will be published later. Reciprocal registration has been granted to John G. Macdonald, of Colorado and F. A. Jackson, of Oklahoma.

New Hampshire.—John R. Kelley, of Newport was recently reappointed for a term of three years, this being his second term.

Following the mid-summer vacation period, the regular meeting of the Board was held at Concord on September 25th. Five candidates were examined and registration was granted to one. Registration by reciprocity was granted to Edwin E. Davidson on Kentucky license.

New Jersey.—Practical examinations were held in Trenton on October 9th, 10th and 11th. The New Jersey Board separates its written and practical examinations, and only those who have passed in all the written subjects are permitted to take the ensuing practical examination.

Reciprocal registration was granted to Bertha R. Fischer on South Carolina license; Charles W. Frantz, Clifford S. Hersh, Paul J. Harris and Edward J. Mack on Pennsylvania licenses.

North Carolina.—Six applications for registration by reciprocity have been accepted by the Board since June 1st, four from South Carolina, one from Florida and one from Virginia.

The next examination meeting will be held at Chapel Hill on November 26th.

Ohio.—At the recent examination held October 15th and 16th, 75 candidates were examined. A meeting is to be held in Cincinnati in November to pass upon grades, and results will then be announced. The following were registered by reciprocity; Kenneth C. Sayre, of Georgia; Roy A. Gohr, of Illinois; Edna F. Nelson, of Indiana; Frank L. Shiley, of Michigan; Gordon C. Robinson, of North Carolina; Maryonette K. Robertson, of Pennsylvania.

We are advised of the death of Inspector C. D. Ferguson; funeral services were held October 2nd.

The State Emergency Board has granted an additional $1000 to continue investigations and prosecutions for the remainder of the calendar year.

Oklahoma.—The following now comprise the Oklahoma Board of Pharmacy: *President*, Cecil G. Steward, Tulsa; *Vice-President*, Albert Eaton, Weatherford; *Treasurer*, W. C. Alston, Checotah; *Secretary*, C. M. Anderson, Oklahoma City; Roy L. Sanford, Enid.

More than one-half the drug stores in the state have already been issued the store registration license required under the new pharmacy law, for which the fee is $10.00. All stores carrying signs "drugs," "pharmacy" or any other term of like import are required to so register, and no license is issued unless a registered pharmacist is in charge of the store.

Pennsylvania.—Examinations were held at the Pittsburgh College of Pharmacy, Pittsburgh, and the Philadelphia College of Pharmacy and Science, Philadelphia, on October 10th, 11th and 12th. There were 146 applicants for registered pharmacist license and 141 for the assistant grade. Results will be announced later.

Reciprocal registration has been granted recently to Harold C. Hanahan, of Georgia; Edward D. Manning, of Illinois; and William B. McKee, of Ohio.

Virginia.—An examination meeting was held in Richmond on Tuesday and Wednesday, November 12th and 13th. Results will be announced later.

Wisconsin.—Out of 119 candidates taking the examination for registered and assistant pharmacist in October, 44 were successful, 31 being registered as pharmacists and 13 as assistants.

The next meeting will be held in Madison on January 20, 1930.

ARIZONA PHARMACEUTICAL ASSOCIATION.

The seventh annual convention of Arizona Pharmaceutical Association was held at Tucson. Among the speakers of the occasion were: President Thomas Roach, of the N. A. R. D., Samuel Antonow and John McPherrin. Secretary Arthur G. Hulett gave a comprehensive account of the activities of the Association and at the conclusion of his report asked that someone be elected in his place. The Association assented to everything that the Secretary said, but not to his resignation; the members insisted on his continuance in the office and he agreed.

The officers elected for the ensuing year are: *President*, F. C. McAlpin, Kingman; *Vice-President*, J. Robertson, Phoenix; *Secretary*, Arthur G. Hulett, Phoenix.

The 1930 meeting is to be held at Prescott during the latter part of September or beginning of October.

THE SECTIONS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

ABSTRACT OF THE MINUTES OF THE SESSIONS HELD IN RAPID CITY, SO. DAK., AUGUST 26 TO 31, 1929.

(See also brief summary reports, Final Session House of Delegates, printed in October JOURNAL.)

SCIENTIFIC SECTION.

The First Session of the Scientific Section, A. PH. A., was convened at 3:30 P.M., August 28th, by Chairman James C. Munch. First Vice-Chairman H. A. Langenhan presided during the reading of the Chairman's address.

THE CHAIRMAN'S ADDRESS.

BY JAMES C. MUNCH.

The Scientific Section of the AMERICAN PHARMACEUTICAL ASSOCIATION is an outgrowth of the Section on Scientific Papers which was established in the early days of the ASSOCIATION. At that period, some half dozen papers of a scientific character were presented during one of the annual sessions of the ASSOCIATION. The development of various phases of pharmaceutical interest and the consequent overcrowding of the ASSOCIATION program finally led to the creation of a number of separate Sections. The scientific papers were diverted into a Scientific Section. For the past several years complaints have been increasing that the Scientific Section program is greatly overcrowded. Two groups have been organized as independent units—the Plant Science Seminar and the Symposium on Genus Mentha. Even so, about sixty papers are offered annually to this Section. The By-Laws specify that not more than ten minutes shall be allotted to the presentation of each paper, and not more than five minutes for discussion. If every author were present and the full period of fifteen minutes used for each of sixty papers, a simple calculation shows that fifteen hours would be necessary for papers, beside the time spent in the transaction of the business of the Section. Each paper represents earnest thought and time, and should receive proper consideration and recognition. Because of the overcrowding of the general AMERICAN PHARMACEUTICAL ASSOCIATION program, it is difficult to arrange for more than two meetings of the Section, in addition to the Joint Meeting with the Section on Practical Pharmacy to discuss U. S. Pharmacopœia and National Formulary Revision problems and progress.

Membership in the AMERICAN PHARMACEUTICAL ASSOCIATION automatically carries with it membership in the Scientific Section. No formalities, examinations or qualifications for scientific or professional standing are imposed, as many of the other professional societies have instituted. The Scientific Section, as now constituted, serves solely and only as a clearing house for about sixty papers at two meetings of the Section during the AMERICAN PHARMACEUTICAL ASSOCIATION convention. During the interval between meetings, the chief task of the officers is to prepare appeals for papers for the next meeting. There has been some coöperation between workers in different fields of scientific study in the investigation of a common problem. However, many of the papers presented each year are unrelated, incomplete and at times startling conclusions are offered which subsequent work fails to verify. As a result of these conditions, the scientific standing of this Section leaves much to be desired.

To consolidate all the scientific work of the ASSOCIATION within the bounds of the Scientific Section, I would recommend—

1. That arrangements be made to combine the Plant Science Seminar and the Annual Symposium on Genus Mentha with the Scientific Section; that their programs be printed as a portion of the program of the Section; and that such papers as seem fitting be transferred to their programs. Arrangements whereby they meet at times which do not conflict with the meetings of this Section decrease congestion and should be encouraged.

To permit better grouping of papers along a general theme, I would recommend—

2. That all papers, together with a short (100–150 words) abstract, be in the hands of the Chairman or Secretary of the Section not less than four weeks before the date of the annual meeting. In case any author does not expect to be present to deliver his paper he should notify the officers and this should be stated in the printed program. In the absence of any author, the abstract of his paper should be read by the presiding officer in order that papers along a common theme may be expected at a certain period of the meeting. The present method of grouping papers into chemical, pharmacological, pharmacognostical and bacteriological groups has proved useful and should be continued.

3. That there be established an additional group embodying work on the general application of scientific principles to pharmacy. This group should not conflict in any way with the scope of the Section on Practical Pharmacy. A survey of the present membership of the Scientific Section should be made to determine into which of the five general subdivisions each member desires to be placed: (1) Bacteriology, (2) Chemistry, (3) Pharmacognosy and Botany, (4) Pharmacology and Bioassays and (5) Pharmacy.

4. That the Chairman and Secretary be authorized to assign a period of time for the presentation of each paper which appears suitable and justifiable to them, based upon the nature of the paper and abstract submitted for their consideration, availability of lantern projection apparatus, blackboards, etc., and the total number of papers to be presented.

Membership in a Scientific Society carries with it responsibility, as well as honor which is valuable in direct proportion to the difficulty of attainment and retention. Full membership should be based upon a certain amount of professional standing and training. Accordingly, I would recommend—

5. That some minimum qualification be established for full membership in the Scientific Section.

Experience in all scientific research has shown that coördinated, coöperative investigation yields the most profitable results. A thorough study of any problem is possible only when hearty coöperation from workers in a number of allied fields of scientific endeavor is obtained. I would therefore recommend—

6. That plans be developed for a coöperative investigation of one product each year by the entire membership of the Scientific Section; this investigation to be under the direction of the officers of the Section, assisted by a representative from each of the five subdivisions; that a single source of material be designated and adequate supplies placed in the hands of each collaborator within a reasonable time after each annual meeting; that all collaborators complete their studies within about three months and promptly submit reports to the subdivision representative for consolidation; that these representatives search the literature pertinent to their fields and consolidate this information with the collaborators' reports into a comprehensive summary; that a symposium be held at the ensuing meeting for presenting results of this collaborative investigation upon authentic material from a common source studied from the bacteriological, chemical, pharmacognostical, pharmacological and pharmaceutical phases; and that these summaries be edited and published as an AMERICAN PHARMACEUTICAL ASSOCIATION Monograph upon the product in question.

As a different product is studied each year, this would lead to a series of authentic, thorough, scientific monographs which will in turn reflect credit and increased scientific recognition upon all participants. Such coöperation would give immediate confirmatory value to analytical procedures, would stimulate productive research and would be available for reference for the U. S. Pharmacopœia, the National Formulary, "New and Nonofficial Remedies" and similar publications. Close contact should be maintained with the National Conference on Pharmaceutical Research, the National Research Council, various committees of the AMERICAN PHARMACEUTICAL ASSOCIATION and research programs of drug manufacturers, schools and Federal and state authorities. Since the members of the AMERICAN PHARMACEUTICAL ASSOCIATION

committees are members of the Scientific Section, there will be no duplication of effort. Actual concrete developments may be confidently expected. Individual investigations will not be prescribed and the present opportunity for the presentation of this type of papers will be continued at the annual meetings. Thus our coöperative efforts will bring scientific standing and recognition to the Section while our individual reports record progress in our individual quests.

First Vice-Chairman H. A. Langenhan appointed the following as members of the Committee on the Chairman's Address: Francis O. Taylor, L. E. Warren and John C. Krantz, Jr.

(While the Committee on the President's Address did not report until August 29th, the report is added here for convenient reference.)

Report of Committee on Chairman's Address.

After careful consideration of the various recommendations made in the annual address of the Chairman of the Scientific Section, your committee desires to report as follows:

Recommendation No. 1.—We recommend that this Section approve the recommendations and that the question be referred to the Council for consideration and such action as they may desire. (This was withdrawn when a resolution embodying the recommendation was acted on in the House of Delegates.)

Recommendation No. 2.—We recommend that the Section adopt this recommendation.—*Adopted.*

Recommendation No. 3.—The committee recommends that the portion of this paragraph concerning the establishment of an additional group of papers be referred to the incoming officers for consideration and action if they so desire. We also recommend that the Section approve the second portion of this recommendation concerning a survey of the membership of the Scientific Section and that the officers of the sections be instructed to take the necessary steps to this end and that if it seems desirable to extend the survey to the entire membership of the ASSOCIATION they proceed as may be necessary.—*Adopted.*

Recommendation No. 4.—We recommend that the Section adopt this recommendation.—*Adopted.*

Recommendation No. 5.—We recommend that a special committee be appointed to study this recommendation and report at the next annual meeting.—*Adopted.*

Recommendation No. 6.—The committee recommends that the Section approve the general idea of this recommendation and that the incoming officers proceed with necessary study and plans for execution of the idea with proper reference of the entire subject to the Council.—*Adopted.*

August 29, 1929.

(Signed) F. O. TAYLOR, *Chairman;* L. E. WARREN; JOHN C. KRANTZ, JR.

The Secretary's Report.

Your Secretary appreciates the coöperation which you have given in making possible this well-rounded program and trusts that you will feel well repaid for your efforts.

(Signed) L. W. ROWE, *Secretary.*

The report was accepted.

Chairman Munch appointed F. E. Bibbins, W. H. Zeigler and F. F. Berg members of the Committee on Nominations.

(*Abstracts of discussions of contributions will be printed when the papers are published, unless some action requires prior publication.*)

The following papers were read and discussed, presented in abstract, or read by title:

"Recent Studies in Molecular Carbon," by Edward Kremers. (Discussion.)

"Assay of Ointment Yellow Mercury Oxide," by L. W. Greene and R. E. Schoetzow. (Discussion.)

"Olive Oil, Fluorescence in Ultraviolet Light," by L. Deuble and R. E. Schoetzow. (Discussion.)

"Food as a Preventive Medicine," by E. A. Ruddiman. (No discussion.)

"Comments on U. S. P. Test for Rhapontic Rhubarb," by R. A. Konnerth and R. E. Schoetzow. (No discussion.)

"An Empiric Assay for Compound Pills of Mercurous Chloride," by L. E. Warren. (No discussion.)

"Amino Alcohols: 4. Reactions with Alkaloidal Reagents," by J. C. Munch and W. H. Hartung. (No discussion.)

"Amino Alcohols. 5. A Potentiometric Study of Certain Homologues of Ephedrine," by John C. Krantz, Jr., and W. H. Hartung. (No discussion.)

"Methylene Blue, U. S. P. as Precipitant of Irish Moss," by George E. Ewe. (Abstract.)

"The Mercuration of Phthaleins in Neutral Solution with Bichloride of Mercury," by F. R. Greenbaum. (Abstract.)

"Methoxyl Content as a Criterion of the Composition of Creosote," by D. V. Sickman and R. P. Fischelis. (Abstract.)

"Aluminum as a Substitute for Zinc in the U. S. P. Test for Arsenic," by E. A. Southworth, E. O. Prather, Jr., and W. F. Ambroz. (Abstract.)

"Gleditschia Triacanthos Linné, a Preliminary Report on the Chemistry of the Fruit," by Loyd E. Harris. (Abstract.)

"Quantitative Analytical Methods for the Study of Peroxide Formation in Ether," by R. Van Winkle and W. G. Christiansen. (Abstract.)

"Catalytic Dehydrogenation of Iso Propyl Alcohol," by W. A. Lott and W. G. Christiansen. (Abstract.)

"The Preparation of Cyclopropane," by W. A. Lott and W. G. Christiansen. (Abstract.)

"Studies of the Analysis and Chemistry of Neoarsphenamine. II. Studies on the Chemistry of Sodium Formaldehyde Sulphoxylate and Their Relation to the Structure of Neoarsphenamine," by Alfred E. Jurist and W. G. Christiansen. (Abstract.)

"Coal Tar Food Colors," by Seward E. Owen. (Abstract.)

"Ultraviolet Transmission of Liquids," by Ellery H. Harvey. (Abstract.)

"Reaction between Formaldehyde and Hydrogen Peroxide and a Quantitative Method Based Thereon," by Arno Viehoever and K. Shinohara. (Abstract.)

The session was adjourned to meet Thursday, August 29th, at 9:00 a.m.—The reading of papers was continued.

"The Bioassay of Capsicum and Chillies," by James C. Munch. (Discussion.)

"The Anthelmintic Qualities of Pepo and Cucurbita Pepo," by James S. Neely and Edward D. Davy. (Discussion.)

"Notes on Cascara Sagrada," Milford J. Harris and Edward D. Davy. (Discussion.)

"Further Studies of the Cat-Eye Method for the Bioassay of Mydriatics and Miotics," by J. C. Munch. (Discussion.)

"The Delicacy of Chemical and Physiological Tests for Strychnine," by J. C. Munch and J. C. Ward. (Discussion.)

"Bioassay of Aconite and Its Preparations. 2. The Comparative Toxicity of Tincture and Fluidextract of Aconite to Guinea-Pigs and Rats," by J. C. Munch and R. I. Grantham. (Discussion.)

"Bioassay of Aconite and Its Preparations. 3. The Pharmacology and Pharmacognosy of Various Species of Aconitum," by J. C. Munch and H. H. Crosbie. (Discussion.)

"Digitalis Assay Standards," by L. W. Rowe. (Discussion.)

"The Pressor Assay of Epinephrine-Novocaine Mixtures," by J. C. Munch and W. A. Deckert. (Discussion.)

"The Pharmacology of Ergot with Respect to Biological Assays and Standards," by Marvin R. Thompson. (Discussion.)

(A statement was made by the Chairman regarding the paper and discussion—that it has been a scientific presentation and all personalities have been intentionally excluded.)

"Comments on the Paper 'The Pharmacology of Ergot with Respect to Biological Assays and Standards,' " by H. H. Rusby. (Discussion.)

On account of the absence of Paul S. Pittenger, the Section elected the Chairman as delegate to the House of Delegates.

Presentation of papers was continued:

"The Effect of Certain Hypoglycemic Drugs upon the Seedlings of Lupinus Albus," by John C. Krantz, Jr. (No discussion.)

"Red Squill Powders as Specific Raticides," by J. C. Munch, E. E. Horn and J. Silver. (No discussion.)

"Amino Alcohols. 3. The Potentiation of the Action of Epinephrine by Arylpropanolamines," by J. C. Munch and W. H. Hartung. (No discussion.)

"A Comparison of Methods for Demonstrating Healing of Rickets in the Biological Test for Vitamin D," by C. F. Church and J. R. Lockwood. (Abstract.)

"Assimilation of Vitamin A When Dissolved in Liquid Petrolatum," by B. Moness and W. G. Christiansen. (Abstract.)

"The Vitamin Potency of Various Grades of Cod Liver Oil," by W. S. Jones and W. G. Christiansen. (Abstract.)

"The New Remedy Business: Its Uses and Abuses," by F. E. Stewart. (Abstract.)

"Studies of Astringency: A Method of Measuring Astringency," by E. R. Theis. (Abstract.)

"Effect of Digitoxin on the Heart of Daphnia," by Arno Viehoever and A. McReyya. (Abstract.)

"Effect of Digitonin on the Heart of Daphnia," by Arno Viehoever and M. Teubis. (Abstract.)

"Transparent Life," by Arno Viehoever. (Abstract.)

"The Therapeutic Activity of Neoarsphenamine," by Alfred E. Jurist and W. G. Christiansen. (Abstract.)

"The Assay of Pancreatin," by F. E. Wilson. (Abstract.)

"Critical Remarks on the U. S. P. Pancreatin Assays," by F. E. Willson. (Abstract.)

The session was adjourned to meet Thursday, August 29th, at 4:00 p.m.

The report of the Committee on the Chairman's Address was read. (See report following Chairman's Address.) On motion by F. E. Bibbins, seconded by F. W. Nitardy, and a vote the report of the Committee was approved. (See also recommendation No. 1.)

The report of the Committee on Nominations was read and held for action until the next session of the Section.

Reading of papers was continued.

"A Thought on the Place of Volatile Oils in Plant Economy," by Frederick E. Marsh. (Discussion.)

"Report on a Splendid Example of Coöperative Research," by Josiah C. Peacock. (No discussion.)

"A Comparison of the Tissue Toxicity and Germicidal Power of Germicides," by Lester C. Himebaugh and Emil C. Fanto. (Discussion.)

"Botanical, Pharmacological and Chemical Study of the Root and Stem Bark of Viburnum Rufidulum," by H. W. Youngken, J. C. Munch and F. J. Amrhein. (Discussion.)

"Medicinal Herbs of the Great Smoky Mountains," by K. E. Bennett. (By title.)

"Native Drug Plants of Nebraska," by E. T. Stuhr. (Abstract.)

"Pacific Coast Drug Plants," by E. T. Stuhr. (Abstract.)

"Oregon Drug Plants," by E. T. Stuhr. (Abstract.)

"An Investigation of Oregon-Grown Peppermint," by Alice H. Hayden and E. T. Stuhr. (Abstract.)

"A Phyto-Chemical Study of Pycnanthemum Miticans (Mountain Mint)," by H. W. Werner. (By title.)

"Polypodium Occidentale (Licorice Fern)," by F. J. Goodrich. (Discussion.)

"A Preliminary Study of the Constituents of Anaphalis Margaritacea," by E. C. Baillie and Nellie Wakeman. (By title.)

"Comments on U. S. P. X Test for Rhapontic Rhubarb," by R. A. Konnerth and R. E. Schoetzow. (Discussion.)

"Black Chokeberry Bark, Aronia Melanocarpa var. grandifolia as a Recent Substitute for 'Shonny Haw,' " by H. W. Youngken. (Discussion.)

"Study of Peppermint Oil Grown in the State of Washington," by A. A. Levine and C. H. Rayburn. (Abstract.)

"Umbellularia Californica, Nutt," by F. A. Nielson and H. M. Burlage. (Abstract.)

"The Seed of Euphorbia Marginata, Pursh," by L. E. Harris and Margaret Gallagher. (By title.)

"Histology and Microchemistry of Digitalis Seed," by Arno Viehoever and K. Shinohara. (Abstract.)

"Pharmacognosy of Psyllium Seed," by Arno Viehoever and E. L. McLaughlin. (Abstract.)

The Section then adjourned to meet in joint session with the Section on Practical Pharmacy and Dispensing.

JOINT SESSION SCIENTIFIC SECTION AND SECTION ON PRACTICAL PHARMACY AND DISPENSING.

The Joint Session of the Scientific Section and the Section on Practical Pharmacy and Dispensing was called to order by Chairman P. H. Dirstine of the Section on Practical Pharmacy and Dispensing on August 29th at 8:00 P.M. The first order of business was the report of the Committee on Pharmaceutical Research presented by Chairman H. V. Arny. (It is printed on page 968 of the September JOURNAL.) The next number of the program was the report of the Committee on Colored Glass Containers presented by Chairman H. V. Arny. (It is printed on page 958 of the September JOURNAL.)

The next order of business was the presentation of the report on U. S. P. X, presented by Chairman E. Fullerton Cook.

REPORT ON THE U. S. P. X.

BY E. FULLERTON COOK.

Because of the intense interest of pharmacy and the AMERICAN PHARMACEUTICAL ASSOCIATION in the Pharmacopœia it has grown to be a customary feature of the annual meeting of the A. PH. A. for the Chairman of the Committee of Revision to make a report on the work of revision.

This report is, therefore, a Chairman's report and does not necessarily express the views of the entire Committee but the opportunity given at these meetings for a general discussion of many pharmacopœial questions has been of great value in establishing wise judgments concerning U. S. P. policies.

As is to be expected the close of a decade and the near approach of another Pharmacopœial Convention greatly stimulates the interest in Pharmacopœia matters.

The Pharmacopœial Committee has always invited full and free discussion of questions of policy and of fact; especially the latter which is, after all, the backbone of pharmacopœial usefulness.

The policies have been the result of slow evolution, they represent the combined judgment of one hundred and ten years of experience and earnest and honest thinking and should not be carelessly overthrown.

The Pharmacopœia of the United States has not always experienced smooth sailing throughout its long existence. A few may still remember the bitter criticisms of the 1870 Revision as I have found it recorded in history, and know of the demand at that time for an entire change in ownership and policy. It was the master mind of Charles Rice and his associates who saved the situation and established a new model for the U. S. P. which is still largely followed and is the admiration of all pharmacopœia makers.

Many remember the stormy days of 1910 and, from past experience are willing to trust the future to the wisdom and sane judgment of a large group of professionally-minded scientists assembled in serious conclave. Surely we may safely trust the ultimate decision of our own democratically organized Pharmacopœial Convention call for May 13, 1930.

Pharmacopœial Publicity.

One crying need is a constant maintenance of pharmacopœial facts before the physicians. The complaint is often heard from pharmacists that the young doctors are not taught enough therapeutics and pharmacology, that they learn their materia medica from the "detail man" and he only talks "specialties."

It is true that the old "materia medica" chair is gone in Medical Colleges but is it necessary to take time in a crowded medical course to teach the student the appearance of crude drugs, their botanical names and habitat? Its place is rightly taken by the new chair of therapeutics

and pharmacology which teaches the action of drugs. Here emphasis should be placed upon the reliable standard remedies, proved by hundreds of years of experience. It is to me a remarkable discovery that of the more than 300 (305) individual therapeutic agents (that is, simple substances and not preparations) now official in the U. S. P. X, 114 were official in the U. S. P. of 1820 and that there was included in the primary list such modern remedies as aconite, aloe, alum, ammonium chloride, belladonna, benzoin, calcium carbonate, camphor, cantharides, capsicum, cinchona, colchicum, colocynth, calumba, copaiba, digitalis, elaterin, ferrous sulphate, nutgall, gentian, mercury, ipecac, jalap, kino, lobelia, magnesium sulphate, myrrh, nux vomica, opium, phosphorus, podophyllum, tartar emetic, guaiac, rhubarb, castor oil, scammony, squill, senega, senna, mustard, sodium borate, stramonium, sulphur, oil of turpentine, veratrum viride, zinc oxide, zinc sulphate, ginger, etc.

It is interesting to note that the 1820 Pharmacopœia relegated to the secondary list the following: Ergot, menthol, quinine and its salts, morphine and its salts and cocaine and its salts.

In explanation of the secondary list of the 1820 Pharmacopœia the editor, doubtless Dr. Lyman Spalding, wrote:

"Preface to U. S. P. 1820.

> The fault of the lists of the Materia Medica which have been adopted in different countries, has always been their redundancy, rather than their deficiency. The number of articles necessary for the management of diseases, and especially of those which any individual physician actually employs, is always very far short of the catalogue afforded by most Pharmacopœias. Besides, as the progress of medical discovery continually tends to the introduction of new articles into use, the Materia Medica must soon grow to an unmanageable size, if its enlargement be not followed by a corresponding retrenchment of superfluities. In consequence of reasons of this sort, many articles contained in European books have been omitted in the American Pharmacopœia. These omissions have been made only where the articles in question were considered inert, or where they were abundantly superseded by substitutes more powerful and more accessible. But, as it happens in most countries, the number of simples occasionally employed in practice is much greater than it suits the proper compass of a Pharmacopœia to contain. In the present work, those native articles have been introduced which were considered to possess qualities sufficiently important, or which were found to be so much employed by practitioners, as to give them any claim to the character of standard medicines. With a view of discriminating between articles of decided reputation or general use, and those, the claims of which are of a more uncertain kind, the Convention determined to refer to a secondary list such substances as were deemed of secondary or doubtful efficacy, retaining only on the principal list articles which might be considered of standard character."

Whose fault is it that the Pharmacopœia to-day and its approved remedies are not in more extensive use by physicians and why are "specialties" being so much more largely known and used? Part of the answer may be that which is so often charged against the medical schools, namely, that they do not devote enough time to the consideration of remedies, and consequently the new physician is not familiar with the Pharmacopœia and National Formulary.

But would this not apply equally to specialties? The fact is that the pharmaceutical manufacturers accept this as an opportunity and send their detail men and their literature directly to the doctor in his office and teach him to use their specialties.

If pharmacists are not making or dispensing official medicines of the right quality, and if they are not taking these to their physician friends in exactly the same way the detail man is doing, upon whom does the blame rest if the doctor uses the "specialty" and has forgotten the standard remedy which was spoken of by his professor in his student days?

There is no question of the value and efficiency of official remedies when they have been properly made and standardized and when the dispensing pharmacist has intelligently supervised their quality and preservation and hundreds of splendid pharmacists throughout the country can testify to the willingness on the part of physicians to talk about these remedies and use them when confidence is inspired by the personality, integrity and ability of the druggist. The success

of the professional side of the pharmacy is dependent upon the personal factor just as much as the success of the skillful doctor.

Excellent programs of U. S. P. and N. F. propaganda have been planned and it is the belief of the writer that to-day there is an unexcelled opportunity for its success, with many pharmacists thinking and planning for the future of real professional pharmacy. The Board of Trustees of the U. S. P. Convention have made a small beginning in this program by accepting an invitation from the A. M. A. for the past five years to present a Pharmacopœial exhibit in the Scientific Section at their annual meeting. These have been prepared and exhibited by various Pharmacy Colleges located in the vicinity of the meeting and have been a distinct success, twice receiving the highest prize among the educational exhibits.

A movement has been successfully worked out for two years in Pennsylvania, whereby professional pharmacy has made a scientific exhibit at the annual State Medical Meeting. This was made possible by an invitation from the State Medical Society. This should spread into every state and be made a regular activity of the State Pharmaceutical Association and able pharmacists must be present throughout the meeting to talk about official products and pharmaceutical service.

This statement is preliminary to an invitation to the Pharmacy Colleges of the United States to coöperate in an exhibition proposed for the Eleventh Decennial Pharmacopœial Convention in Washington next May. This has been authorized by the U. S. P. Board of Trustees.

About forty individual exhibits are proposed. In one of these, the history of the Pharmacopœia and its revision methods will be presented; in several others, it is hoped that the several Government laboratories, coöperating with the Pharmacopœia, will make individual displays indicating the character of their activities and in the remainder of the booths pharmacy colleges are being invited to make effective and original exhibits of Pharmacopœial drugs, chemicals and preparations, classified according to their therapeutic activity. It is also hoped that this exhibit may subsequently be used as the basis for a booklet which may be largely used in promoting a knowledge and use of Pharmacopœial drugs.

The Extent of Use of Formerly Official Drugs.

The deletion of a title from the Pharmacopœia on the grounds that, in the opinion of the Committee, its value "is of a more uncertain kind," as Dr. Spalding so quaintly expresses it, always leaves open the course of reinstatement in a subsequent edition, should later developments indicate a mistaken judgment.

The Committee of Revision is earnestly desirous of checking this phase of revision, that authentic facts may be available to guide the new Committee. With this in view, a questionnaire, covering all medicinal drugs, chemicals and preparations official in the U. S. P. VIII and IX, but not admitted to the U. S. P. X, has been prepared. It is interesting to note that about 55 per cent (205) of these titles, are now official and consequently standardized in the National Formulary V.

A study of this list, however, shows a distinct defect in the present method for providing medicinal standard under the Food and Drugs Act. In the main, the U. S. P. and N. F. cover the uncontrolled medicinals used in medicine in the United States but when a drug or chemical is deleted and there are no preparations of that "simple" in common use, the present N. F. does not recognize or standardize it.

The seriousness of this situation is evident when this deleted list is examined and we find no standard for such articles as diluted hydrocyanic acid, bismuth betanaphthol, crude calcium sulphide, monobromated camphor, cerium oxalate, diastase, sodium cyanide, strontium bromide, strontium iodide, etc.

The writer has several times suggested as one remedy for this situation the widening of the scope of the National Formulary so that simple drugs and chemicals may be included and standardized even if not used in a formula. There would seem to be no serious objection to this broadening of the N. F. field, especially as it already includes and standardizes hundreds of "simples." A change of title to "National Formulary and Standard," is all that is required to take away the limiting character of the present title. If this were done, the two books would function perfectly in their respective fields.

The active help of pharmacists throughout the country is urged in the securing of data concerning to-day's use of these substances.

Additions to the Pharmacopœia.

It will also be helpful to the next Committee of Revision if pharmacists and doctors suggest medicinals of the "Newer Materia Medica" which are suitable for admission to the next revision. This is also covered by the questionnaire just referred to, copies of which may be obtained by dropping a card to the Chairman of the Committee. Extensive publicity concerning this study will be given through the medical and pharmaceutical press during the next few weeks, and inviting the coöperation by physicians and pharmacists.

It may be of help to note that the 1929 edition of "Useful Drugs" of the A. M. A. includes the following unofficial titles: Ethylene for anesthesia, insulin, neocincophen, spirit of ether, solution of aluminum subacetate, sulpharsphenamine, tuberculin, streptococcic-scarlatina antitoxin, diphtheria toxin-antitoxin, antimeningococcic serum, antirabic vaccine, staphlococcic vaccine and typhoid vaccine.

The decade is drawing to a close—it has seen splendid coöperation between medicine and pharmacy in every phase of the revision—a true and equal partnership—and with each profession doing the utmost in their several fields of scientific service, we may properly anticipate in the future, a greater influence and importance for our Pharmacopœia in the effort to prevent and cure disease, than in any previous period of the century.

Following the report, Chairman Cook called attention to papers which had been distributed to the members giving a list of the titles of the official preparations. He also distributed questionnaires, and stated that the various medical and pharmaceutical publications had been invited to discuss the questionnaire. As wide distribution as possible of these questionnaires is desired; the Chairman said that every possible way for securing lists of those who are interested in the revision of the Pharmacopœia would be secured and questionnaires mailed. He explained that the questionnaire made inquiry of physicians relative to the drugs in use, and pharmacists were asked to what extent certain drugs and preparations were called for over the counter. An analysis will be made of the list and reports made thereon. These questionnaires have been devised as a means for securing knowledge for the Committee on Scope of the next Committee of Revision.

The next order of business was the presentation of the report on the National Formulary by Chairman Wilbur L. Scoville. (The report has been printed in the October number of the JOURNAL on pages 1037–1044.)

The report of the Committee on the Pharmaceutical Recipe Book by Chairman J. Leon Lascoff was read by E. Fullerton Cook.

On motion duly seconded the reports were received and referred for publication. (The report on the Pharmaceutical Recipe Book will be printed in this or a succeeding issue of the JOURNAL.)

Chairman Dirstine asked Chairman James C. Munch to preside during the remainder of the session. Chairman Munch called for the report of the Committee on Ebert prize. It follows:

Report of the Committee on Ebert Prize.

> "The Committee recommends that the Ebert Prize for 1929 be awarded to J. C. Krantz, Jr., of Baltimore, Md., for his paper on, "The Buffer Capacity of Acacia and Tragacanth," as presented before the Scientific Section of the AMERICAN PHARMACEUTICAL ASSOCIATION at the Portland, Maine, meeting."

The closing feature of the Joint Session was the presentation of two papers constituting a Symposium on Bacteriology. The first paper was that by George F. Reddish on "The Antiseptic Action of U. S. P. and N. F. Ointments" and the second paper by L. E. Himebaugh on "Reddish Germicidal Test on Antiseptics of U. S. P. and N. F." (Both papers were illustrated by lantern slides.) The papers are to be printed and the discussion thereon will be included. After the reading of these papers the Joint Session was adjourned.

SECOND SESSION.

The Second Session of the Scientific Section was convened by Chairman Munch at 2:00 P.M. August 30th. The first paper of the program was "A Study of the Stability of Solution of Arsenous and Mercuric Iodide U. S. P. X," by W. J. Husa and W. W. F. Enz. (Discussion.)

President Jones introduced Frank D. Kriebs, Secretary of Agriculture for South Dakota, who spoke briefly. Secretary Kriebs is a graduate in pharmacy of Northwestern University in the class of 1899. He stated that the Department of Agriculture had the enforcement of pharmacy laws in charge and all other legislation that applies to the drug business in the state. He regretted his inability to participate in the Convention to a larger extent because he had an engagement in another section of the state.

Chairman Munch expressed appreciation of the Secretary's visit.

Reading of papers was continued:

"The Influence of Light upon the Hydrogen-Ion Concentration and Stability of Certain Pharmaceuticals," by John C. Krantz, Jr., and C. Jeleff Carr. (Discussion.)

"Suggestions Relative to U. S. P. X Revision," by Jules Bebie. (Discussion.)

"VI. The Standardization and Stabilization of Veratrum Preparations: The Hydrogen-Ion Concentration Factor," by E. E. Swanson and C. C. Hargreaves. (Discussion.)

"VII. The Standardization and Stabilization of Ergot Preparations: The Hydrogen-Ion Concentration Factor," by E. E. Swanson. (Discussion.)

"Stability of Anæsthetic Ether in Containers of Various Types," by E. Van Deripe, L. W. Greene and R. E. Schoetzow. (Discussion.)

"Rennin: Its Deterioration and Comments on the N. F. V, Monograph," by L. D. Havenhill. (Discussion.)

"Studies on the Acid Base Equilibrium of Tincture of Digitalis," by John C. Krantz, Jr. (Discussion.)

"Effects of Buffering the External Phase upon the Stability of Emulsions," by John C. Krantz, Jr. (No discussion.)

"The Bellier Test for Sesame Oil," by E. Fullerton Cook. (No discussion.)

"Evaluation of Pharmaceutical Glassware," by N. Storm and James C. Munch. (No discussion.)

Haziness of Final Chloroformic Extractions in Alkaloidal Assay," by George E. Ewe. (Abstract.)

"Comments on Some Tests and Assays of the U. S. P. X," by Herbert C. Kassner. (Abstract.)

Secretary John C. Krantz, Jr., of the National Conference of Pharmaceutical Research stated that he had no report but requested that the Scientific Section continue its coöperation.

Chairman James C. Munch reported that E. N. Gathercoal had been elected *Chairman* of the Conference, John C. Krantz, Jr., reëlected as *Secretary* and Philip I. Heuisler as *Treasurer*. The meeting of next year is to be held in Baltimore about the time of the meeting of the A. PH. A.

A motion was made by F. W. Nitardy that a Board of Review on Papers for Presentation and Publication be provided.

It was voted that a Committee be appointed by the incoming chairman to study this matter and report at the Baltimore meeting.

The report of the Committee on Nominations was called for and the following officers were nominated:

Chairman, H. A. Langenhan, Washington.
First Vice-Chairman, E. E. Swanson, Indiana.
Second Vice-Chairman, W. J. Husa, Florida.
Secretary, L. W. Rose, Michigan.
Delegate to the House of Delegates, James C. Munch, Maryland.

The nominees were elected and thereafter duly installed. The retiring Chairman, James C. Munch, thanked the members for their coöperation and the incoming Chairman, H. A. Langenhan, expressed his appreciation of the honor conferred and asked for the support of the membership.

The Scientific Section was then adjourned.

SECTION ON PRACTICAL PHARMACY AND DISPENSING.

The First Session of the Section on Practical Pharmacy and Dispensing was convened at 9:00 A.M., August 29th by Chairman P. H. Dirstine.

Secretary H. C. Newton presided while Chairman Dirstine read his address.

CHAIRMAN'S ADDRESS.

BY P. H. DIRSTINE.

Your Chairman first wishes to express his appreciation of the honor conferred upon him when you elected him to the chairmanship of this Section at the Portland meeting, which he was unable to attend.

"I realize that there are a goodly number of most excellent papers to be presented before this Section, and I have no desire to present a lengthy address. I will, therefore, confine myself to a few remarks and suggestions of a practical nature.

"For a number of years there has been, from year to year, a greater number of pharmaceutical preparations put out by manufacturing firms, who in turn solicit the doctor through detail men and encourage the doctor in the dispensing of ready-prepared medicines. In many cases these ready-to-take medicines are like ready-to-wear clothes, they fail to fit the patient. Of course, this is the doctor's concern; but let us look at this from a pharmacy standpoint. We find an ever-increasing number of high-priced products on which the druggist is forced to charge a high price, but pays him a small per cent of profit. In my opinion, every effort should be made to encourage doctors to use the U. S. P. and N. F. preparations more extensively than at present, and also to encourage doctors to build up formulas of their own to prescribe. I believe that every encouragement should be given to strengthen the courses of Materia Medica, Therapeutics and Pharmacology in our medical colleges, to the end that graduates in medicine may be better able to prepare combinations of U. S. P. and N. F. drugs to suit the needs of their individual patients, instead of being practically dispensers of patent and proprietory medicines, a tendency with many doctors of to-day.

"We frequently hear of drug clerks being discharged because of dishonesty, and many proprietors complain that they are unable to find honest clerks. We oftentimes find on investigating these cases and charges, that the clerk is drawing a salary of $110.00 to $115.00 per month—a salary that the proprietor would not think of trying to live on, yet he expects his clerk to do so. I am wondering if it is not about time that druggists, as proprietors, should begin to realize that a drug clerk is a human being, and when they pay salaries of this kind they themselves contribute to the cause of the troubles of which they complain. A pharmacist who has spent three or four years in college, and has had some experience, should not be expected to work longer hours and for less salary, than is paid the untrained shoe clerk, grocery clerk and others in like positions. I am certain that when druggists pay their clerks salaries in keeping with their professional training and skill, the cases of dishonesty will be greatly lessened.

"I hope that this Section, at this session, will pass a resolution condemning the special registration feature of some State Boards of Pharmacy, wherein they require schools of pharmacy to register with their State Board, in order to make the graduates of that school eligible for reciprocation, or to take the state examination in that state. It seems to me that if the membership of a college of pharmacy in the American Association of Colleges of Pharmacy means anything, it should mean more than the very meager requirements of various State Boards of Pharmacy. When the American Association of Colleges of Pharmacy puts its approval upon a college, by giving it full membership, in my estimation, that should fulfill the requirements permitting the graduates of that school to appear before any Board of Pharmacy for reciprocal registration, or to take the examination in that state, provided experience and character requirements are met.

"Recently, one of my own graduates from the four-year course in pharmacy was denied the right to appear before a State Board in the Middle West, because of the fact that our school had neglected to register with, and fill out a set of blanks required specifically by that State Board of Pharmacy. When the blanks were received it was found that our school was so far in advance of this state's requirements, that it was amusing, necessitating that the blanks be nearly made over in order to set forth our present requirements. I think this is a requirement for which there

is no justification, and should be a relic of the past. I sincerely hope that pressure may be brought to bear, to the end that requirements such as these, be abolished, and when one wants to know if a school of pharmacy is of high class, that he may turn to the official membership list of the American Association of Colleges of Pharmacy and, if the name appears there, let it be recognized as meaning something; that its requirements are not less than, but equal to, or above those of any State Board. In other words let us lend our support to the proposition that the American Association of Colleges of Pharmacy shall set the pharmaceutical educational requirements for this country. Laws for reciprocal registration should be uniform throughout the land, and should be based upon a national inspection.

"The prescription pharmacist is especially interested in the style and type of container in which the product of the manufacturer is marketed, be it a bottle or a package. For the products sold directly to the consumer this is of less importance, but for those products used exclusively by, or frequently prescribed by physicians, the style of package is of utmost importance. I shall give a few illustrations to make clear my point. If a doctor wishes to dispense certain proprietaries in the original package, he is unable to do so even though he disguises the odor, and colors the product, because of the fact that the name of the product, as well as the name of the manufacturer is blown in the bottle. Neither can the druggist use the bottle for the dispensing of any other product when the bottle is empty, because of the same reasons, as well as the peculiar shape of the bottle. On the other hand if we have a call for another preparation on a prescription, we place the bottle under the tap, the label comes off readily and we have a perfect prescription bottle; note the saving in time and expense. Should the bottle be returned for refill on a prescription we can dispense anything desired in it, or place it in stock as a new bottle. In the case of capsules, ampuls, etc., the same is equally true. As an example: I have a well-known capsule package in mind. All that is necessary in the dispensing of them is to open the package, remove the circular enclosed, apply your own label, which if of standard size covers completely the written material on the package, making a perfect dispensing package. As to a highly undesirable dispensing package, I have in mind another ampul package; a more ill-conceived package for dispensing purposes is hard to imagine, and yet, it is used practically exclusively on doctors' prescriptions. If we could encourage manufacturers to package their products for dispensing in plain and serviceable containers for the trade, be it in liquid or solid form, we would eliminate a national waste and save the pharmacists of this country thousands and thousands of dollars, every month.

"I have tried to call to your attention a few simple present-day needs of a practical character. Perhaps one or two of them may seem at first out of place being presented here before this Section, nevertheless they concern the every-day practice of pharmacy, and I hope they may merit your consideration.

"In closing I express my thanks and appreciation for the most excellent manner in which our secretary, Dean H. C. Newton, has carried on the work of his office, and I know we will all enjoy the splendid program he has been instrumental in arranging for us. I also wish to thank the contributors to the program of this Section, as it is through them and their efforts that this Section is able to present from year to year its interesting and instructive programs."

Abstract of Discussion.

John Culley stated that he had never dispensed a proprietary preparation in its original bottle or package; that invariably the containers of the store were used for prescriptions.

He was surprised to learn that any Board of Pharmacy would turn down a candidate from a well-equipped college.

In reply Chairman Dirstine said that a number of states require a signed application before the candidates are eligible.

Mr. Culley said that the requirements for reciprocity are based on what the state requires and not on the qualifications of the candidate. He said the N. A. B. P. has instituted a survey of pharmacy. A beginning has been made by the effort to study the schools of pharmacy.

W. J. Husa asked whether it would not be better to discuss this address after the Committee on Resolutions made a report.

The Acting Chairman stated that he realized there might be considerable discussion at the present time which would be repeated after the report of the Committee has been made.

After further discussion by Messrs. Fuhrmann, Gray and Newton, it was decided to defer action on the Chairman's address until after the Committee on Resolutions, to which the recommendations of the address were referred, had been heard from.

Chairman Dirstine then resumed the Chair and called for the report of the Secretary.

REPORT OF THE SECRETARY.

BY HOWARD C. NEWTON.

To the members of the American Pharmaceutical Association:

The By-Laws of the Section on Practical Pharmacy and Dispensing state that the report of the Secretary shall be brief and that it shall have as its subject the condition of the Section. Complying with these requirements I would report that, in my opinion, this Section is enjoying a state of dormant health—if such a condition is possible. I have found a keen interest in the work of this Section exhibited by nearly all member pharmacists with whom I have corresponded. Such interest surely indicates the health of the Section. However, there is a noticeable hesitancy on the part of most of these pharmacists when it comes to presenting at our meetings the results of work that they may have done in attempting to solve some of the problems in practical pharmacy and dispensing. It is this hesitancy that causes me to characterize the health of the Section as dormant. It has been said that there is a tendency on the part of research workers "to accumulate a superabundance of facts and data and to devote too little time and effort in the proper correlation and interpretation of them." Perhaps this tendency has caused some of our members to hesitate in offering the results of their work in the interpretation, correlation and application of facts and data, fearing that such are not "in style," no matter how valuable they may be in practice.

I believe that it is one of our duties to make the practicing pharmacist realize that he is in a preferred position in the matter of solving problems in practical pharmacy and dispensing and, furthermore, that he owes it to his profession to give other pharmacists the benefit of the results that he has obtained in solving these problems. While I have some very definite ideas as to how this improvement can be accomplished, I do not feel that this is the proper time to express them. I will merely state that from my position as Secretary I am confident that it will not be difficult to change the present condition of dormant health to one of very healthy activity within the Section.

After some discussion the report, on motion of P. H. Utech and seconded by John Culley and a vote, was referred to the Committee on Resolutions.

A paper was presented by P. Henry Utech entitled "Some Official Preparations."

Abstracts of discussion of contributions will be printed when the papers are published unless some action requires prior publication.

The following papers were presented:

"Clinical Laboratory Work a Prescription Aid," by Lee S. Coy. (Discussion.)

"A Prescription Containing Guaiac and Acacia," by John. C. Krantz, Jr., and C. Jeleff Carr. (Discussion.)

"Commercial Aspects of Professional Pharmacy," by H. S. Noel. (No discussion.)

Chairman Dirstine appointed as members of the Committee on Nominations—Louis Saalbach, of Pennsylvania, J. L. Powers, of Michigan and Gustav Bachman of Minnesota; as members of the Committee on Resolutions—Clyde M. Snow, Illinois, Wm. H. Glover, Massachusetts and C. M. Brown, Ohio.

The First Session of the Section on Education and Legislation was then adjourned.

The Joint Session with the Scientific Section was held August 29th, 8:00 p.m. For program see Scientific Section.

SECOND SESSION.

The Second Session of the Section on Practical Pharmacy and Dispensing was called to order by Chairman P. H. Dirstine at 3:30 P.M. The reading of papers was continued:

"A Survey of the Prescription Business in Buffalo," by Leon Monell. (By title.)

"A Method for the Qualitative Estimation of Chloroform Liniment," by Alfred C. Anderson. (By title.)

"Preparation of Enteric Capsules," by S. L. Hilton. (Discussion.)

"Preparation of Ampuls," by S. L. Hilton. (Discussion.)

"A New Explanation of an Old Incompatibility on That of Glycerin and Sodium Borate," by Charles W. Bauer. (Discussion.)

"Pharmaceutical Practicalities," by Robert J. Ruth. (No discussion.)

"Prescription Bottles," by W. J. Husa. (Discussion.)

"Who Is to Blame?" by J. Leon Lascoff. (By title.)

Chairman Gustav Bachman reported for the Committee on Nominations as follows: *Chairman*, H. C. Newton, Nebraska; *Vice-Chairman*, Charles V. Netz, Minnesota; *Secretary*, E. O. Leonard, Idaho; *Delegate to House of Delegates*, John C. Krantz, Jr., Maryland. The nominees were elected in regular order.

The report of the Committee on Resolutions was presented by Clyde M. Snow. The Committee recommended that the address of Chairman Dirstine be referred to the Committee on Resolutions of the House of Delegates and approved the report of the Secretary. After considerable discussion on motion duly seconded and a vote the report of the Committee was accepted (see pages 1088 and 1089). The reading of papers was continued:

"Physicians Prescriptions in Relation to the U. S. P. and N. F. Preparations," by P. J. Kolb. (Discussion.)

"A Further Study of the Incompatibility of Sodium Bicarbonate and Sodium Salicylate," by John C. Krantz, Jr., and C. Jeleff Carr. (Discussion.)

"The Manufacture and Dispensing of U. S. P. Digitalis Preparations," by Robert P. Fischelis. (By title.)

"The Advance of Pharmacy in California," by P. W. Howard. (By title.)

"A National Welfare Fund," by Edward Swallow. (Discussion.)

The Final Session of the Section on Practical Pharmacy and Dispensing was then adjourned.

SECTION ON EDUCATION AND LEGISLATION.

The First Session of the Section on Education and Legislation, A. PH. A., was convened by Chairman A. L. Winne, at 9:00 A.M., August 29th. Charles E. Mollett presided during the reading of the Chairman's address. It follows:

THE CHAIRMAN'S ADDRESS.

BY A. L. I. WINNE.

It is customary for the chairman of this Section to render a report, or make an address, and while I would gladly pass by this portion of our program and devote the time to the splendid papers which we have on our program, I suppose I may not do that, so will do the next best thing and will address you very briefly.

The program of this Section is devoted to discussion of matters of educational interest and those of legal and legislative importance, and an examination of our tentative program this year discloses that we have an unusual range of subjects and many distinguished speakers to present them. I wish here to commend our efficient secretary on his good work in enlisting these speakers, and to thank the speakers who will follow for their interest in the work of the Section.

The ground which I could cover in this paper appears to me to be well covered in the papers which appear on the program, and I would not take advantage of the prior position which I hold on the program to go into a discussion of the subjects selected by those who are interested enough to prepare papers and come here to present them.

I may briefly touch on one or two matters, however, without trespassing, I hope, on the ground covered by speakers who follow me. I have been interested in Pharmacy Corps legislation during the past year, and without going into details of what has been done or what we hope to do, I merely want to express my gratitude for the help rendered me as chairman of the committee handling that matter by the members of the committee associated with me, and to say a word or two about the splendid assistance given the committee by Secretary Kelly. In reality Secretary Kelly did most of the work and the rest of us merely gave a helping hand on occasions. Of the progress of the legislation and the hearing held before the Congressional Committee, you will be told, I believe, by one of the speakers on our program.

Looking further at the program I find that four other speakers will discuss legislative matters, such as "The Parker Bill," "Prohibition and Food, Drug and Insecticide Law," while another will talk about matters partly legislative and partly educational. The educational side will be treated from the point of view of educating the public relative to pharmacy, teacher training, training men for the neighborhood stores, failures before State Boards and the work of the junior colleges in relation to pharmacy education. Perhaps this Section has in the past had programs better balanced than this one, but I doubt it. I hope we will gather the maximum from our several sessions.

So much for the program which is to follow.

Now, if I may use a few minutes more, I would like to go back to the matter of legislation looking for better pharmacy in the Army of the United States. Without encroaching too much on the speaker who will talk about this matter, I would like to draw attention to the fact that this legislation is a matter which is of great importance to pharmacy, and is one worthy of the interest, active interest, of all who hold pharmacy worth while. Our bill will be introduced at the next regular session of Congress and if it is to become a law it will require the whole-hearted efforts of all who wish to see pharmacy advance. It will not be enough to wish the committee and our secretary well in the fight to be made. Each and every pharmacist in this organization must dig in and do a part of the fighting. This can be done by arousing the interest of the pharmacists of your own state and locality, and by getting in touch with your Senators and Representatives and presenting the matter to them so that they will understand what it is all about if the issue comes to a vote, as we hope it will. The influence which you can bring to bear from your own state outweighs anything which ASSOCIATION officials can do, and it will depend on what you do whether this bill ever becomes a law. The organizations of pharmacy have done what they could do in the way of giving approval and going on record in favor of the measure. This is useful, but by no means all-sufficient. The voters back home still have the voice of the masters. A piece of work yet remaining to be done, to a large extent, is enlisting the aid of such patriotic organizations as the American Legion, Veterans of Foreign Wars and like ex-soldier bodies. These have a large influence, and can be reached in each state best by those who live in these states.

Passing from the legislative to the educational phase of our work, I hope you will bear with me a little bit longer, while I touch briefly on a phase of the teaching of pharmacy which may not be of a great deal of interest to some of you, and which may even be regarded by some as taboo in this Section. I want to talk about the teaching of Commercial Pharmacy, or, if you prefer, as one speaker attending our annual meeting termed it "So-Called Commercial Pharmacy." What we call it makes little difference.

If you will pardon again personal reference I may state that from a number of years of experience in pharmacy work, retail, wholesale and board and association work, I have been able to view matters from more than one side, and I have, like most of you, come to recognize that the commercial activities of the pharmacist constitute a fairly large part of his activities, and I believe that he should be trained to perform these commercial duties as well as to perform his professional duties. It is my opinion that in the schools of pharmacy as operated to-day he is being well trained for his professional work and miserably trained for his commercial work. There are, of course, exceptions. Many schools are making real headway in this field, but much remains for the best of them to take on and do well.

Early this year I undertook a limited survey of the work being done in commercial pharmacy by the schools which are members of the American Association of Colleges of Pharmacy. To a questionnaire sent out to all of them thirty-five replied, and their answers boiled down to a few words disclosed that almost all of these attempted to teach commercial pharmacy in some fashion, some using textbooks and others not using any, and very few of them devoting anything like adequate time to the subject. I could give you an array of figures on various phases of the replies returned, but I am not going to do that. In bringing this to your attention I have in mind the hope that the schools will wake up to the urgency of properly training the men whom they turn out as graduates, to go into drug stores and work, so as to make these men more useful to the men who employ them, more useful from the start. A school has not done anything approaching a finished job when it turns out a pharmacist trained for only half the work which will be expected of him by his future employers, or which he will have to do for himself if he enters

the drug business. I believe that I am extremely liberal when I say half the work may be of a professional type. Many say that his professional work does not constitute twenty-five per cent of his activity, and others rate it at ten per cent or less. Whatever is correct, in the large majority of instances, it certainly is a fact that more than ninety per cent of the graduates of schools of pharmacy engage in retail drug work. Why not recognize that as a fact and train the men to meet the conditions which will confront them as soon as they leave college?

The failure of many schools to do this work properly is to be attributed, I believe, to the fact that the men who are teaching in these schools do not know very much about the conducting of a retail drug store and assume an attitude which they may use as a shield for themselves and their own ignorance of the matter by saying that it is not the province of a school of pharmacy to teach commercial subjects. There are, of course, two sides to the question. Some, I know, interpose honestly conceived objections. I respect their attitude, while differing radically with their conceptions. The majority of schools teaching pharmacy are trying to accomplish something along commercial lines, and the greatest weakness in this work at the present time is that the efforts being made are too feeble, and this is so, I think, because the men who are trying to teach these subjects are not properly qualified to teach them. They have no background of their own, in a commercial way, and try to put the subject over by brushing up superficially on some of the high points of the commercial phase of pharmacy. That will never lead very far. It is a case of the blind leading the blind.

Commercial pharmacy, and that is just another way of speaking about the whole field of retail merchandising, has as many sides and facets as has professional pharmacy, and it is to-day the phase of the drug business which all too often is paying the freight for the whole enterprise. Without in any manner attempting to minimize the importance of professional pharmacy, because I believe that that in itself is the solid rock on which the drug business is moored, I do believe that the schools could do the drug business a great service, and in that way do pharmacy a service, if they would wake up to the fact that there is a bread and butter side to the game which their graduates must play in after-life, and seriously attempt to equip those graduates to enter the fight without unnecessary handicap.

In my humble judgment Commercial Pharmacy is worthy of a place alongside Professional Pharmacy throughout the three- or four-year course given by any school, and it is worthy of the services of teachers trained in the subjects which they essay to teach. Few schools of pharmacy in the United States to-day are taking this matter very seriously. I do not hesitate to predict that eventually every school of pharmacy which hopes to survive as such and to have any following will be forced to wake up to the needs of the times and make proper provision to meet them.

L. D. Havenhill moved that the Chairman's address be accepted. The motion was seconded by A. H. King, and carried by vote.

Secretary Glenn L. Jenkins, of the Section, reported that the large number of papers make it advisable to limit the maximum time allowed for presentation and discussion.

(*Abstracts of discussions of contributions will be printed when the papers are published unless some action requires prior publication.*)

The presentation of papers followed. The first item of this part of the program was a discussion of the Parker Bill by E. F. Kelly. (To be printed; see also resolutions page 950, September JOURNAL.)

The first paper of the program is entitled "What the Food, Drug and Insecticide Administration Is Doing for Pharmacy," by L. E. Warren. (See October JOURNAL, pages 998–1004.)

Other papers presented were the following:

"The Proposed Transfer of Prohibition Enforcement from the Treasury Department to the Department of Justice," by James H. Beal. (See pages 1028–1031, October JOURNAL.)

"Student Branches, A. PH. A.," by B. V. Christensen. (Discussion.)

"Pharmacy Needs an Objective Policy," by R. L. Swain. (See pages 1016–1020, October JOURNAL.)

"Teacher Training in Pharmacy," by E. T. Motley. (No discussion.)

"What the Pharmacist May Do for Himself," by E. C. Brokmeyer. (See pages 1020–1024, October JOURNAL.)

A discussion followed on Publicity and Pharmacy Week, participated in by Messrs. Maxwell, Kemp, Brokmeyer and Walton.

Chairman Winne appointed a Committee on Nominations composed of R. L. Swain, B. V. Christensen and M. N. Ford. The First Session of the Section on Education and Legislation was then adjourned.

SECOND SESSION.

The Second Session of the Section on Education and Legislation was called to order by Chairman A. L. I. Winne at 2:30 P.M., August 30th.

The Chairman stated that Dr. James H. Beal had been requested to draw up a resolution and asked for its presentation at this time. (The resolution is printed on page 950 of the September JOURNAL.) The Section by vote approved the resolution.

Reading of papers was continued:

"Bromatotherapy and the Drug Store," by L. F. Kebler. (No discussion.)

"The Neighborhood Store—How to Train for It," by Wortley F. Rudd. (Discussion.)

"Many Candidates Fail State Board Examination in District No. 3. Why?" by Rudolph H. Raabe. (Discussion.)

"Comments on the Revocation of Permits Issued under the National Prohibition Act," by W. Bruce Philip. (Discussion.)

"The Junior College in Relation to Pharmaceutical Education," by Frederick J. Wulling. (By title.)

"Educating the Public on the Profession of Pharmacy," by D. B. R. Johnson. (By title.)

"Summary of Regulations Governing the Sale of Drugs and Medicines in Sweden," by Knut Sjöberg. (See pages 896 to 902, September JOURNAL.)

The Committee on Nominations presented the following names of the officers for the ensuing year: *Chairman*, Glenn L. Jenkins, Maryland; *Vice-Chairman*, B. V. Christensen, Florida; *Secretary*, Rudolph H. Raabe, Ohio; *Delegate to the House of Delegates*, Wortley F. Rudd, Virginia. The nominees were elected in due order. The Final Session of the Section on Education and Legislation was then adjourned.

SECTION ON COMMERCIAL INTERESTS.

The First Session of the Section on Commercial Interests, A. PH. A., was convened by Chairman R. B. Rothrock at 4:00 P.M., August 28th.

Chairman Rothrock stated that he would not take up the time of the Section by delivering an address because of the business before the Section, and Secretary Joseph G. Noh reported on the status of the Section on Commercial Interests. He regretted that there were not more papers but felt assured that the quality would make up for the number.

Chairman Rothrock appointed the following as members of the Committee on Nominations: Leonard O'Connell, B. M. Keene and Charles J. Clayton; of the Committee on Resolutions: Fred W. Meissner, W. Bruce Philip and A. C. Taylor.

The reading of papers was proceeded with.

"An Old Fashioned Drug Store in a Modern Setting," by Thomas Roach. (See pages 1014–1016, October JOURNAL.)

"The Ethics of Commercialism." (No discussion.)

"The Independent Retail Drug Store a National Necessity," by R. E. Lee Williamson. (Discussion.)

The First Session of the Section on Commercial Interests was then adjourned.

SECOND SESSION.

The Second Session of the Section on Commercial Interests was convened by the Chairman, R. B. Rothrock, at 8:30 P.M., August 29th. The reading of papers was proceeded with.

"A Five-Foot Shelf of Journals," by E. H. Niles. (See pages 1013, 1014, October JOURNAL.)

"What is the Matter with the Drug Business and What Is to Be Done about It?" by Charles J. Clayton. (Discussion.)

"Dividing Your Inventory to Find Your Proper Rate of Turnover," by W. Bruce Philip. (Discussion.)

"Taking the Prescription Department Out of the Red," by H. S. Noel. (No discussion.)

"Why not Establish a Regular Fee for the Pharmaceutical Profession," by Edward Swallow. (By title.)

"Shall the Independent Druggist Sink or Swim? It Depends upon His Initiative and Effort," by H. W. Heine. (No discussion.)

"Keeping Independent," by Edward S. Rose. (No discussion.)

"Activities of Druggists Research Bureau," by E. L. Newcomb. (Referred to the Committee on Resolutions.)

The Committee on Nominations reported the following names for officers of the ensuing year: *Chairman*, Denny Brann, Iowa; *Vice-Chairman*, Joseph G. Noh, Nebraska; *Secretary*, Rowland Jones, South Dakota; *Delegate to House of Delegates*, R. B. Rothrock, Indiana.

In regular order the nominees were elected.

A motion was made and carried thanking the retiring officers; the Section was then adjourned.

SECTION ON HISTORICAL PHARMACY.

The First Session of the Section on Historical Pharmacy was convened by Chairman Lyman F. Kebler, at 3:30 P.M., August 22nd.

The Chairman announced that he would present a sketch of James Henry Shepard, in place of the usual formal Chairman's address.

JAMES HENRY SHEPARD, B.S., M.A.[1]

BY LYMAN F. KEBLER,

one of his admiring pupils.

HUMANITY AND HERO-WORSHIPERS.

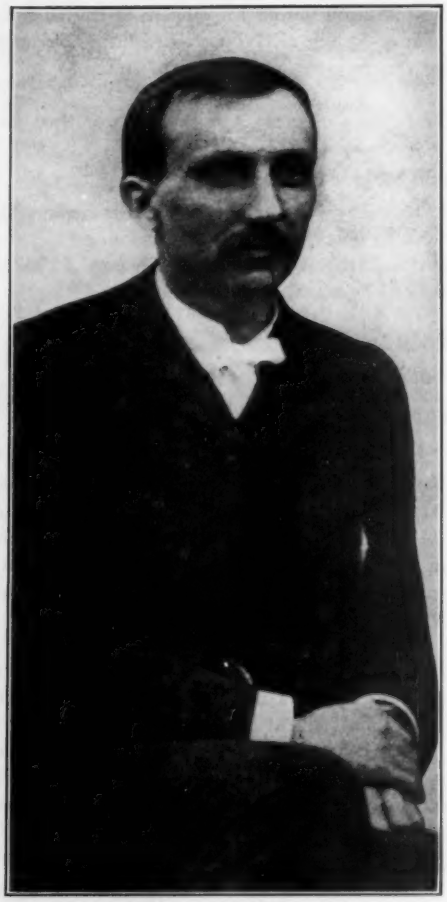
I am a hero-worshiper. Hero-worshiping is an inexpressibly precious fact. It stimulates world activity. Much of history is based on it. Hero-worship exists everywhere from Divine adoration to the humblest practical recess of life. Most human lives are influenced for better or worse by our heroes, large or small. The folk-lore of nations embodies much hero-worship. Nations are in a measure built up and around its heroes—civil, military, political, religious, educational, poetic, scientific, professional, dramatic, athletic and aeronautic. We all have our Washingtons, Jeffersons, Lincolns, Roosevelts, Napoleons, Platos, Socrates, Prescotts, Procters, Remingtons, Lindberghs, etc., but the most potent heroes, are those who mold our characters during the formative periods of our lives; our parents, our teachers and those who aid us in the development of our avocations, whether business, professional, educational or otherwise.

James Henry Shepard is one of my heroes. He, a stranger, called me Lyman and made me feel at home. I am probably Prof. Shepard's oldest living pupil who followed in his footsteps as a chemist, particularly along lines of pure foods and drugs. Our work often brought us together and it gives me very great pleasure and pride to relate briefly, at this meeting held in his adopted state, the manner in which he influenced my career; his eminence as a chemist, a beloved teacher and a good citizen; his contact with pharmacy; his excellent work for pure foods and his investigations of agricultural problems that he dealt with for more than a third of a century. I first met him face to face as Principal of the Saline High School, one of the units of the wonderful Michigan State Public School system, when I applied for admission in 1879. I may have met him while he was a student in the University of Michigan and I, a lad, playing under its eves. I heard of and saw many of the pranks of the University students long before I entered the Saline High School. I well recall the kindly and sympathetic manner in which Prof. Shepard plied me with questions; a sun-burnt, horny-handed, rough-shod, frightened farmer's lad, just released for school by my father, after the fall's work was pretty well along for the winter. All farm boys know what the fall work means. Some also know what it means to begin school work in the middle of the term, as we called it then. It is no child's play, but grit and determination were with me. I was a Red School House protégé. We there learn self-reliance. Give and take was part of our training.

I now understand Prof. Shepard's interest in me. He was likewise a farmer's lad with similar environment. He was born April 14, 1850, the son of a pioneer Michigan farmer who died

[1] The First Professor of Chemistry and Pharmacy of the South Dakota State College.

during the boyhood of his son, who was raised by relatives and friends. My education was acquired in a short-term unorganized country school where the teacher taught and disciplined all comers. My teachers were all mighty fine women. They taught me ABC, reading, writing, arithmetic, geography and some algebra. How well the work was done in our little red school house is shown by the fact that the generous-hearted principal entered me without a condition. This was a great compliment to my teachers and made me feel very proud. Professor Shepard taught physical geography. I selected this study and learned then to admire him. He was my



JAMES HENRY SHEPARD.

LYMAN F. KEBLER.

When James and Lyman Met.

first man teacher. Geography always fascinated me. We studied physical geography in Wilson's Fifth Reader, which was a veritable Bible to me in the country school. I learned many valuable lessons from its pages on Botany, Chemistry, Physics, Physiology and Physical Geography. I still read it with pleasure. It gave me the foundation which made me proficient and gave me standing in my hero's eyes. He told us so many fascinating things about these sciences. His enthusiasm, knowledge and encouragement decided me on a future career but environment stepped in and separated us for how long, no one knew at the time.

SHEPARD MUCH-LIKED IN SALINE.

Shepard was greatly admired in Saline. I can best express it in the following words of Goldsmith:

"The village all declared how much he knew;
'Twas certain he could write and cipher too;
While words of learned strength and thundering sound
Amazed the rustics ranged around—
And still they gazed, and still their wonder grew,
That one small head could carry all he knew."

Shepard obtained his education in the school system of Michigan. The B.S. degree was conferred on him by the University of Michigan in 1876.

My hero left Saline to take up post-graduate work at the University of Michigan and I felt obligated to contribute my earnings to the family chest to help my parents bring up my younger brothers and sisters. The future looked anything but bright, so far as acquiring an education was concerned. Prof. Shepard drifted out of my life. When I was past twenty, my father released me from further contributions, advised me to save my earnings and augment my schooling. The idea was fine but its accomplishment some problem. Where would it be possible for me to get a foothold with some assurance of success, with my limited education at my age? I was employed in the building trade in Ann Arbor and considered attending its high school, but everything, including the building that I often passed, looked so formidable that I could not reconcile myself to undertake the task there. In time (1884) I learned that Prof. Shepard was teaching the sciences in the Ypsilanti High School. He was appointed instructor in 1882. I took occasion to make him a friendly visit. We talked over my problem. He told me that I had a hard task before me but could master it with my stamina, grit and determination. He assured me of his moral support. Later I went to Ypsilanti to start in. Professor Shepard was on hand. He took me to the Superintendent, R. W. Putnam, who later became my staunch friend, explained my problem and vouched for me. The Superintendent entered me with one year's credit. Three more years of school work. Professor Shepard was my mentor. He was the only human being I knew in the city. It looked like a gigantic undertaking. I was strong and husky, with no fear of work, but associating with the small boys and girls who seemed to know so much more than I did was an awful trial. It was my greatest handicap. I took as much scientific work under Professor Shepard as the rules of the school permitted, the first year, including chemistry and physiology. Shepard's "Elements of Chemistry" was just coming off the press in page proof (1884). This greatly enhanced the standing of this genial teacher in my eyes. It practically superceded every small chemical textbook then on the market. We were given advance sheets for class work. The book covered both class instruction and laboratory work, which was highly gratifying to me. I shone in laboratory work. Under the guiding hand of Professor Shepard and the encouragement of other teachers, the year's work was very creditably done. He urged me to continue, suggesting that he would let me do some special work in chemistry under his guidance. I planned to take the county teacher's examination and spend the next year in teaching. The examination was taken. I qualified as a teacher but when fall rolled around, the urge to continue the high school work was so great that all teaching opportunities were passed up. I had earned enough money during the vacation time to see me through another year. My teachers then talked to me about preparing myself for a chemical career, taking the course in the University of Michigan School of Pharmacy. This seemed like building air castles. We talked about it again and again. I dreamed it. Professor Shepard gave me a course in water analysis, taught me in microscopical work and assisted me in making a goodly number of galenicals. This had a great appeal. His personality, urging, encouragement and good wishes, together with the inspirations of my other teachers, won for me a University education. I have brought myself considerably into the picture so far. It brings out a side of our hero's life that many of his students admire. The deep impressions he made on many determined their life work. I shall let others tell more about this later. I am personally unable to more than feebly express my gratitude for the remarkable encouragement and inspiration I received at his hands.

DR. A. B. PRESCOTT AND PROFESSOR JAMES H. SHEPARD.

Albert Benjamin Prescott and James Henry Shepard had similar careers. Both were outstanding chemists. Both were drafted into pharmacy. Both were my revered teachers. A. B. Prescott was professor of Organic and Applied Chemistry and Pharmacy of the University of Michigan at the time Shepard acquired his B.S. degree and undoubtedly sat at the feet of our be-

loved teacher. When Shepard took his post-graduate work, Prescott was dean of the School of Pharmacy. Shepard probably learned his pharmacy from Dean Prescott.

PROFESSOR SHEPARD TAKES UP HIS NEW LABORS.

Professor Shepard, in 1888, identified himself with the South Dakota College and Experiment Station, where he spent the remainder of his busy life. His name appears as Chemist in Bulletin No. 4, issued in July 1888. He was vice-president of the College for ten years, director of the Experimenting Station for six years and chemist for the State Pure Food Commission from 1901 to his death, February 21, 1918. About his new field of labor, he writes, "My appointment as Chemist for the Station was issued in June 1888. At that time the Station had neither laboratory nor appliances. Practically nothing had been done in this department. Instructions were issued to purchase apparatus and chemicals, sufficient to carry on the work." He did the first analytical work in the state. Bulletin No. 8, December 1888, on "The Drinking Waters of Dakota," written by him contains his analyses. The same year he established a course in toxicology. It was also decided by the officials to include courses this year in the curriculum which might assist in the training of students for the position of assistant pharmacists. The catalog of 1888 describes a rather extended course in materia medica. In 1889 the regents officially established a two-year course in pharmacy in the following language:

> "The two-year course in pharmacy is designed to fit young men or women for the business of druggists, and it is hoped that arrangements may soon be made by which graduates from this course may become licensed as assistant druggists."

Professor Shepard at the time, bore the title of "Acting Professor of Chemistry, Physics and Pharmacy." The late, brilliant Cyril G. Hopkins, one of his esteemed pupils assisted him. Professor H. B. Matthews, of whom we shall hear later, at present—Professor of Physics in the South Dakota State College—was assistant in the pharmacy laboratory. There were ten in the first graduating class, in 1890. With the appointment of Bower T. Whitehead as Professor of Pharmacy in 1897, Professor Shepard devoted his entire time to the various chemical problems that arose.

The following published in the Ypsilantian, Ypsilanti, Michigan, August 14, 1890, is of interest to Rapid City and probably explains why Professor Shepard did not accept the deanship of the South Dakota School of Mines, located at Rapid City: "A private letter from Professor McLouth of Brookings, South Dakota, informs us that Professor J. H. Shepard was offered the deanship of the Dakota School of Mines at Rapid City with a salary of $2500, but after visiting Rapid City in the 'Hills,' where the school is located, he had decided not to accept." The train, on which the Professor was, was "held up" in Nebraska by robbers, and an enforced contribution levied on the passengers, so it seems that the Professor is compelled sometimes to watch a system of "re-actions" not known to chemistry.

Many of the delegates to this convention will go over the same route, traveled by Professor Shepard to the city in the "Hills," nearly thirty years ago, and it is hoped there will not be any holdups.

SOME OF PROFESSOR SHEPARD'S OUTSTANDING WORK.

He gave special attention to the control of nitrogen in cereals and the milling and analyzing of macaroni wheat, introduced into the state by the U. S. Department of Agriculture. This involved the investigation of bleached flour, concerning which he made an international reputation for himself. He testified in a number of court cases brought under the Federal Food and Drugs Act against flour bleachers, conducted a hearing before the U. S. Secretary of Agriculture, on the subject, and was called to the English Courts to testify against flour bleaching. The bleachers lost, but most white flour on the market at present, in the United States, is still bleached.

Shepard was among the first to make a systematic analysis of whisky. His report, entitled, "The Content of Whisky," 1906, has been translated into many modern languages. It laid a foundation for judging whisky. At the meeting of the State Food and Dairy Commissioners, held in connection with the St. Louis Exposition in 1904 and later meetings of the association, he reported on the harmful effects of preservatives and dyes on digestion. His papers and exhibits attracted world-wide attention. The Commissioners delegated him to represent the pure food interests at the hearing before President Taft in 1909, for the purpose of determining "What is

Whisky?" I was present when some of these activities took place. He is the author of many bulletins covering the examination of waters, foods, forage plants, sugar beets and macaroni wheat. He developed a superstrain of beets; in fact, he is credited with growing the world-record sugar beet, containing 26.2% of sugar by weight.

SHEPARD, A WORTHY, THRIFTY CITIZEN.

He gave the world three fine citizens, two boys and one girl; was an elder in the Presbyterian Church; a Bible class teacher for many years; a 32nd degree Mason and a member of many other organizations. His wife Clara, still living, was a wonderful helpmate. He owned a valuable quarter section of land near the College and gave special attention to the breeding of thoroughbred registered stock. His herd of Duroc Jersey swine was one of the best in the West. He also grew macaroni seed wheat for Government experiment.

HEAR WHAT SOME OF HIS OTHER PROTÉGÉS SAY.

Shepard had a keen, analytical and judicial mind, yet in the class room his personality counted most. His enthusiasm and zeal were contagious. He possessed the essentials of an ideal teacher, with a unique style often tinctured with humor. Even students unfit to grasp the intricacies of chemistry welcomed his lecture hour. To a notable degree, he molded the careers of the better students. A goodly number became chemists or physicians. I am well aware that my presentation of the influence and work of our beloved, amiable teacher and colleague is most inadequate, but will let others amplify the encomiums to which I shall say *amen*.

Dean E. R. Serles writes, "While he was not actively associated with the Department of Pharmacy after 1897, he was vitally interested in the work at South Dakota State College and gave many of the graduates of Pharmacy opportunities to do special work in the Experiment Station Laboratory. I count myself particularly fortunate, having served in such capacity during the last four years of his life."

Listen to the interesting story told by H. B. Matthews, at present Professor of Physics in the South Dakota College:

"I feel that I had a rare privilege in having been a student under Professor Shepard and later an Assistant in his department. During the early days of State College Professor Shepard not only had the Chemistry but the Pharmacy. C. G. Hopkins gave the instructional work in Pharmacy while Professor Shepard and myself looked after most of the laboratory work. While my success as a teacher may not be phenomenal, still I feel that such success as I have had is to a certain extent due to my many years of close companionship with Professor Shepard and my observations on his methods. Of course, I do not do things as he did. No one could do that. He had a personality and a uniqueness of presentation peculiarly his own. I have often wondered at his uncanny ability to hold the attention of students. His peculiar habits caused you to watch him. His word pictures were skillfully presented. His humor was contagious. His mind was keenly analytic. He was able to figure what the other fellow was going to do, which was evidenced many times during the political turmoils that affected the state and educational institutions of early days in South Dakota.

"I have mentioned his keen sense of humor. He often illustrated something in the text by a story. His preliminary actions, before actually telling the story, had the interest of the students aroused and often they would be laughing in anticipation before the story began.

"May I say personally that Professor Shepard meant a great deal to me and his memory is still precious. He did more for me than any other man in helping me to a start in life. His suggestions and advice were always timely. All students that came in contact with him were inspired to continue in their work. I know that Dr. C. G. Hopkins, as long as he lived, almost worshipped him. This is true of such men as Dr. Adams Dutcher, Pennsylvania State College; Dr. Guy Youngberg, University of Buffalo; Dr. F. A. Coller, University of Michigan; State Chemist L. E. Walter, University of Wyoming, etc.

"I believe that no one questions but that he was a real chemist. As you will remember he had a very large nose. I have often thought that it was as useful as it was large for he could come nearer telling what things were by the sensation of smell that any man that I ever saw."

Grant Houston, M.D., pharmacy class of 1890, adds some personal touches.

"I have a picture of the first class in pharmacy, graduating in the spring of 1890, the group

with Professor Shepard in the center. There were ten in the class. I remember him as a very pleasant but rather firm teacher and my most intimate recollection of him in the class room is his sitting at the end of the room on a high stool and his position on the stool was stooped forward, stroking his tiny moustache and I distinctly recall the peculiar facial expression he had when answering one of our quesitons in chemistry or waiting our reply to some chemical question.

"He was a very kindly man and a splendid teacher, one who always wanted the work done in an exact and prompt manner. I remember that he asked one of the members of the class, Will Bentley, to do something in the chemical work for him but he saw by Bentley's expression that he did not quite get Shepard's point and after explaining it for a while to him, he turned away and said, 'Here, Houston, you can do it quicker than I can explain to Bentley what I want done.'

"He was always interested in sports and life of young people, particularly those in his classes. He was an untiring worker and a man whose soul was tied up in his profession."

Irwin D. Aldrich, Secretary of the Pierre (South Dakota) Commercial Club, reminisces excellently about our hero.

"I entered college at Brookings about the first of March 1889, which was then the middle of the school year. I classified as a pharmacy student, and jumped into the middle of the course in physics, taught by Professor Shepard. I had had some physics and was able to do this. He also taught the class in pharmacy. The first work we did in this was in determining specific gravities, which gave us some practice in handling the balances.

"I came from the farm to college with the supposition that college professors would use language in ordinary instruction which it might be difficult for a farm boy to understand. In this respect Professor Shepard was a disappointment. In fact he had so many old yankee farm expressions that he was a continual delight to me. The simplicity with which he would state a proposition made all his students like him. I remember when we were studying sound he once said, 'Now if you take a piano key and kindo tunk on it,' etc. I recorded some of these in one of my school books, but it was destroyed by fire.

"Professor Shepard had a habit of throwing in bits of simple philosophy from time to time, before a class. He had been a student of Richard Olney, in Michigan, the mathematician and author of textbooks in mathematics. Something came up in class once which caused him to digress with a reminiscence about as follows:

"Now this man Olney was a kind of a h-a-r-d-h-e-a-d-e-d, p-r-a-c-t-i-c-a-l man, a-f-t-e-r-a-l-l, and he said to us once, in class: 'If you don't learn anything else in college, except not to be afraid of a man because he is a college graduate, the course will be worth *something* to you.

" 'And he chuckled in the peculiarly Shepardian way.'

"Our relations were always very pleasant, and later on as a member of the Board of Regents and as secretary of the Board, viewing his work from a little different angle, I continued my high opinion of the man.

"Speaking of the attempt that was being made in those days to show that the word wine as used in the Bible meant the unfermented juice of the grape, he once said, 'Why that was rediculous. Look what it did to Noah.'

"Our 1890 Pharmacy class had for its motto *Nulla vestigia retrorsum*. He looked at it quizzically, chuckled, and said, 'Aldrich, I hope that is no reflection on the efficacy of the physic you boys will dispense.' "

Even a short biographical sketch like this, requires no small amount of effort and research, but it is well worth while in both pleasure and thrill, to say nothing of the justice to those who have gone to the promised land of human perfection and the good it may be to future generations. In closing may I urge others to engage in this line of endeavor.

Chairman Kebler exhibited pictures of Professor Shepard and a photograph of himself taken at the time he entered the pharmacy school. He then called upon Dean E. R. Searles of the Division of Pharmacy of South Dakota State College, also a student of the late Professor Shepard, who presented the following:

SOME REMINISCENSES OF PROFESSOR SHEPARD.

BY E. R. SERLES.

It was my good fortune to be very intimately acquainted with Professor Shepard for a good many years. I took my work in pharmacy at South Dakota, majoring in chemistry, and carried out

the major portion of my work in chemistry under him. One of the more recent pictures Dr. Kebler has shown is the last picture taken of Professor Shepard in the laboratory. It was in connection with his work done with sugar beets. He did extensive work on them for twenty-seven years. He pioneered in their development from a low percentage of 10 or 11 per cent with cross-breeding bringing it up to a final average of 18.2 per cent. A good deal of that work was done at the Bellefourche project, which lies sixty miles northeast of Brookings, and is a development of the Orman dam, which is one of the largest earth dams in America. This development reached its climax in the successful development of one strain, one breed of which reached the world's record of 26.2 per cent. I was working in the laboratory when that beet was analyzed.

One picture shows the crude machinery which Professor Shepard used in boring the beets. It was a sewing machine with the wheel left on and portions of the head taken off, and an auger used for boring.

I do not know whether Dr. Kebler has revealed the number of bulletins published by Professor Shepard at the South Dakota State College. We have twenty-one. There were in all thirty-five. We were unfortunate in losing a great deal of his work through the total loss by fire of our Chemistry Building a little over a year ago. By the titles of these bulletins you can see how diversified were his interests.

Some of the titles are as follows: "The Drinking Waters of South Dakota;" "The Sugar Beet of South Dakota;" "Artesian Wells of South Dakota;" "Deep Wells and Shallow Wells;" "Irrigation in South Dakota;" "Forage and Garden Crops in the James River Valley;" "Drouth-Resisting Forage Plants;" "Nutritive Forage Plants Introduced for Ensilage;" "Marketing Wheat and Its Value in Bread-making."

This last was perhaps the most outstanding work of Professor Shepard. It attracted so much attention that upon the completion of the last two bulletins and his investigation in bleached flour work, he was called to London on the famous Bleached Flour Trial as an expert witness. It is interesting to know that the State flour mill is carrying on work at the present time which is purely a continuation of those experiments started in 1905.

Immediately following that, Professor Shepard went into the question of steam canning in the Pure Food and Drug Laboratory here in South Dakota, which was located at the South Dakota State College at that time.

I presume you will imemdiately link him up when I say he was closely associated with Dr. E. H. Ladd, of North Dakota and Dr. H. W. Wiley. In 1906 came the National Food and Drug Act.

For a long time Professor Shepard was consultant for all experimental work of the South Dakota State College, including the development of food products of South Dakota, various farm crops, and such chemical problems as happened to come in connection with other fields of endeavor.

One bulletin, which I do not have in my possession, which is called for all over America and in all other civilized countries, was the bulletin which he compiled after appointment to the commission of the President of the United States for analysis of sugar. You can readily see why there was such call for it. Immediately following that work, Professor Shepard went to New Orleans on the New Orleans Molasses Trial as a witness to decide whether it was real sorghum or not. His testimony was effective in controlling that product as a food for our tables of to-day.

In his later years—the time I was most closely associated with him—he gave a good deal of time and thought to the revision of one text which he published—"Shepard's Elementary Chemistry"—which was built around an analysis scheme of his own. I am free to say very nearly every inorganic chemistry to-day is modeled closely after his original piece of work. Dr. Shepard's health failed so utterly that he was unable to complete that revision. Thus far, no one has had the time or interest to revise the book.

In personality, I have never met a man with such kindly tendencies toward his fellow men. He was profoundly religious. It is said in his own community, he had a men's Bible class at the First Presbyterian Church for eleven years, and taught it without missing a Sunday. He used to chide us about our ignorance of the Bible when we went for consultation on another problem.

He was not particularly active in many public activities—civic organizations, etc. Rather, he was what you would call a home man, devoted entirely to the service of his home and College.

One rather prominent educator made this comment concerning Professor Shepard. He

said, "He is able to take a scientific subject and discuss it with the average uneducated layman and the scientist, each in his own language, and yet keep them both interested."

I can say frankly to you he is my greatest inspiration as a teacher.

On motion, duly seconded, the two contributions were received for inclusion in this report.

Chairman Kebler then called on the Secretary, Dr. George D. Beal, who stated that he had no formal report to present. He expressed his appreciation for the coöperation of the members of the ASSOCIATION in arranging for the program of the Section. He stated that at least thirty-five, of all persons to whom requests were addressed, were instrumental in getting contributions for this program.

Chairman Kebler remarked that if all other secretaries would do as well as Dr. Beal, in a few years the Section on Historical Pharmacy would have a program that would exceed that of other sections, because there is so much material to work on.

The chairman called for the Historian's report, which follows:

THE HISTORIAN'S REPORT.

BY. E. G. EBERLE.

A memorial tablet in Cramer's pharmacy at Paderborn bears the inscription "In diesem Hause entdeckte 1803, Fr. W. Sertuerner das Morpheum." More recently a memorial plaque was unveiled in the medical clinic of Muenster commemorating the fact that this pharmacist was born in Westphalia in 1783, and that he was the discoverer of morphine. On the 2-mark German emergency note of 1921 there is a picture of Sertuerner and under it these words:

"Deine Huette verfallen, Dein Grab verwest, Dein Werk wird bleiben, so lange die Erde steht."

Sertuerner laid the foundation of alkaloidal chemistry; his discovery was followed soon after by those of other pharmacists. In the closing paragraph of an article by P. J. Hanzlik in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 18 (April 1929), 375–384, we find this statement: "Now on the 125th anniversary of this important discovery, we reaffirm our gratefulness for the timely effort and native talent of the once obscure pharmacist of Paderborn."

In 1879 to 1885 our veteran member, John Uri Lloyd, contributed a series of articles published in the PROCEEDINGS OF THE A. PH. A. which are accredited with laying the foundation of colloidal chemistry. In the JOUR. A. PH. A., 11 (June 1922), 410–423, Part I of "Physics in Pharmacy," by J. U. Lloyd is published and in this Section we have on the program "Physics in Pharmacy. Part II," by John U. Lloyd, Wolfgang Ostwald and Walter Haller; the article is illustrated by sixty half-tones.[1] This work checks up that of the senior author, of fifty years ago; and the subject deals with the forms of menisci; it is largely a review of the work of J. U. Lloyd. The methods employed are more exact than those in the earlier contribution, however, Dr. Ostwald commenting thereon states "Especially it occurs to me that we have perhaps not compared sufficiently the new experiments with the old ones, although we have indeed confirmed almost all of your (J. U. Lloyd's) results by using a more exact method." It is a source of pride that the honored member has contributed his researches to our ASSOCIATION. Incidentally, his 80th birthday was celebrated by Cincinnati in April; there was almost a week of celebration. A Cincinnati daily paper said editorially: "When such a man as John Uri Lloyd celebrates the eightieth anniversary of his birth it is more than a personal event. It becomes a public matter."

Pharmacists of Sweden last year celebrated the 150th anniversary of their organization. The history of their profession, as such, really dates to 1621, when King Gustavus Adolphus granted them royal privileges and stipulated that no new shops were to be opened without authorization by the state. Swedish pharmacists enjoy an equal social standing with physicians. For this meeting in the Section on Education and Legislation we have a paper by Pharmacist Knut Sjöberg, of Stockholm, on "Summary of Regulations Governing the Sale of Drugs and Medicines in Sweden."[2]

One of our honorary members, William Kirkby, presided over the centenary meeting of Manchester Pharmaceutical Association. The Lord Mayor, in congratulating President Kirkby

[1] See JOUR. A. PH. A., XVIII (September 1929), 862–875.

[2] *Ibid.*, XVIII (September 1929), 896–902.

and the Association, commended the objects of the organization—the advancement of pharmacy, the protection of legitimate trade interests and the promotion of fellowship; in motives, the members are actuated by a sense of responsibility, and seek only the public good.

This has been a year of Golden Anniversaries of state associations; as far as our records show, six of these organizations have celebrated the 50th year of their accomplishments—Iowa, Kansas, Illinois, New York, North Carolina and Texas.

Former President George Judisch added $200.00 to the Lillian Judisch Memorial Fund, and contributed an historical account of the Association's activities.

Matt Noll, former president of Kansas Pharmaceutical Association, contributed an historical paper on "Fifty Years of Pharmacy in Kansas." The past-presidents were presented with gold badges.

Curt P. Wimmer gave an illustrated historical account of New York Pharmaceutical Association; pictures of former conventions were shown.

The program of the Illinois Association had a cover of brilliant gold. Secretary Day has prepared a history of the Association, which is part of the program of this Section.

Gold badge buttons were presented to the five living charter members of North Carolina Pharmaceutical Association—E. V. Zoeller, F. W. Hancock, John H. Hardin, F. R. Hood and H. R. Horne; the latter is in his 90th year and still active in pharmacy.

The early records of Texas Pharmaceutical Association were scattered until Secretary Walter D. Adams compiled them into an historical number of the *Texas Druggist*. The work of Secretary Adams deserves commendation; a bound copy of the History together with the Proceedings of the Golden Anniversary Meeting will be presented to the Library of the AMERICAN PHARMACEUTICAL ASSOCIATION. The Association has sponsored a fund to be known as "Texas Fund," for equipping, and as far as possible maintaining, the editorial rooms of the A. PH. A. Headquarters.

Our honorary member, Dr. J. J. Hofman, represented the AMERICAN PHARMACEUTICAL ASSOCIATION at the meeting of the International Pharmaceutical Federation, held during the Jubilee meeting of the National Association of Pharmaceutical Syndicates of France, July 10–12, 1928. Report on formulas of international importance was made by Messrs. Herissey, Greenish and Begium; that on melting and boiling points, by Prof. Dr. Eder and Prof. Dr. Schoorl. Messrs. Collard and Linstead made a number of suggestions for a standard pharmacy law; Prof. Dr. Tiffeneau reported on biologic standards for digitalis preparations, and Prof. Dr. Wasicky on standards for drugs of lesser activities. Stockholm was chosen for the 1930 meeting. A report of the meeting is printed on page 1157 of the November JOUR. A. PH. A. (1928).

The Gesellschaft fuer Geschichte der Pharmazie has added more publications to its list of valuable monographs; a noteworthy number is that by Dr. Leudy, of Switzerland, on alchemical and chemical characters; the book contains 30 illustrations and 128 tables. The former include a number of half-tones of jars and bottles on which the characters are employed to designate the contents. The Society for the History of Pharmacy (France) contemplates for its members the issuance of a *de luxe* edition of some beautiful work. The secretary of the Society is E. H. Guitard.

Thomas Greenish and Professor Dragendorff were largely responsible for the establishment of the Hanbury medal in memory of the late Daniel Hanbury, who was an honorary member of this Association; Professor Dragendorff also was a member of the A. PH. A. Former President, H. H. Rusby, will receive the Hanbury medal in October; and two other American pharmacists have been thus honored—Prof. John M. Maisch and Dr. Frederick B. Power.

The College of Pharmacy of the City of New York, Columbia University, celebrated its centenary in June. The program of the celebration was most interesting; a memorial volume, compiled and edited by Curt P. Wimmer, has been published. Historic Drug Store exhibits were arranged by Dr. J. Leon Lascoff, through whose energy and interest the old apothecary shop and modern pharmacy were made possible. The centenary event was further enhanced by the conferring of the Doctor of Science in Pharmacy degree on Drs. R. A. Hatcher and W. A. Bastedo, Dean F. J. Wulling; Chairman of N. F. Committee, Wilbur L. Scoville, and Charles F. Schleussner, a veteran graduate of the College.

Hugh Mercer's apothecary shop at Fredericksburg, Va., in which General George Washington maintained a desk for twelve years, has been recently restored to its former condition, as

far as this is possible. Strange to say, a side of the room with shelves and bottles thereon was boarded up, presumably for the purpose of keeping that part of the store intact for another apothecary occupant. The building was occupied by others who were not apothecaries and the shelving and bottles remained undiscovered until restoration was recently proceeded with. The work of restoration and maintenance is under the direction of the Citizens' Guild. Reference to the Mercer Apothecary Shop can be found in the June JOURNAL for 1926 and in the September issue of 1928.

The Fifth International Congress of Military Medicine and Pharmacy was held in London, May 17th. U. S. pharmacists were not represented—see June JOURNAL, pages 547 and 611. The reason given is, that Congress made no provision for defraying the expenses of such delegates.

Action was taken at the Portland meeting that the ASSOCIATION should seek to have provisions made for a Pharmacy Corps in the Medical Department of the U. S. Army. The Hearing on the Pharmacy Corps Bill, held on February 20th, gives an account of the evidence presented for the need of a Pharmacy Corps. As much more evidence is in hand it is reasonable to assume that Congress will not ignore the request, because it is right and just, and because reason will not permit the members to ignore the rights of soldiers to the same protection given other citizens. See pages 295–299, March JOURNAL.

"The Production of Pharmacopœias in Various Countries" was the subject of a report of Hugh N. Linstead of the Pharmaceutical Society of Great Britain and Secretary J. J. Hofman of the International Pharmaceutical Federation before the latter body. See JOUR. A. PH. A., 17 (1928), 795–797.

The U. S. Pharmacopœial Convention will assemble in Washington next May for revising the present edition of the U. S. Pharmacopœia. The "Father of the U. S. Pharmacopœia" was Dr. Lyman Spalding, to whose efforts, time, money, energy and persistence the U. S. Pharmacopœia was established. New York University has a Hall of Fame in which men and women who have contributed largely to the welfare of humanity are memorialized. We should see to it that Dr. Lyman Spalding receives the recognition to which he is entitled because of the value of his work to humanity. Nominations will be received February 1st to March 15th and should be sent to Dr. Robert Underwood Johnson, Hall of Fame, New York University. Though Dr. Spalding was not a pharmacist, he recognized the importance of pharmacy. Strong efforts should be made to enlist the interest of medical men and citizens everywhere in this movement; every pharmacist can have a part. The elections are held every five years and only very few are given the distinction.

Dr. John Phillips, member of the Revision Committee of the United States Pharmacopœia was one of the victims of the frightful explosion in the Cleveland Clinic, of which he was the founder.

Nagayoshi Nagai, emeritus professor of the Imperial Academy, Japan, died February 10, 1929, aged eighty-four years. He made many important researches in pharmacology, one of the most notable being the synthesis of ephedrine.

This report would extend beyond its limitations to sketch briefly those of our ASSOCIATION who have ceased their labor among us and, therefore, with few exceptions, only the names of the deceased will be given; the numbers in brackets refer to pages in the issues of the JOURNAL, published since our last annual meeting; they are:

Clarence C. Ballou, Boise, Idaho [308]; Narciso Rabell Cabrero, San Sebastian, P. R. [308]; Harry R. Cameron, Port Deposit, Md.; Fred Welcome Churchill, Proctor, Vt. [58 and 323]; Otto Ferdinand Claus, St. Louis, Mo. [307]; Alfred DeLang, Cincinnati, O. [85]; Wm. Larremore DuBois, Catskill [529]; Mrs. John A. Dunn, Lynbrook, L. I.; John Henry Flint, San Francisco, Calif. [529]; Manuel Bernard Francis, Belmont, Mass.; Harry Tower Galpin, Amityville, L. I.; Henry R. Gering, Plattsmouth, Neb. [308]; John G. Godding, Boston, Mass. [433]; Frank S. Goodman, Washington, D. C. [435]; James F. Guerin, Worcester, Mass. [323 and 434]; Harry W. Harris, Chicago; H. L. Haussamen, Grafton, N. Dak. [407]; H. E. Holmes, Seattle, Wash. [1251]; Thomas N. Jamieson, Pasadena, Calif. [84]; James H. Jones, New York City [530]; Gus C. Kendall, Meridian, Miss. [1251]; James D. King, Haddonfield, N. J.; Charles S. Koon, Muskegon, Mich. [1251]; Erich H. Ladish, Chicago, Ill. [307]; Leroy A. Lallance, Bradenton, Fla. [307]; Ferdinand Luedke, Oak Creek, Colo.; James D. Nutt, Wilmington, N. C. [741]; Charles A. Oats, New York City [195]; Harry Pick, New York City;

John R. Pitt, Middletown, Conn. [1162]; D. W. Ramsaur, Jacksonville, Fla. [195]; Wm. H. Rogers, Middletown, N. Y. [195]; L. J. Schlesinger, Yonkers, N. Y. [530]; Albert Schneider, Portland, Ore. [1161]; C. H. Schoenhut, Cleveland, O. [1162]; F. A. Seaman, Daytona, Fla. [308]; Lorentz A. Seitz, Sappington, Mo. [1162]; Otis W. Smith, Sedalia, Mo.; I. A. Solomons, Savannah, Ga.; T. V. Sords, Cleveland, O.; Louis Carl Staudt, Aurora, Ill. [307]; Wm. P. Thomason, Guntersville, Ala. [1251]; Michael Uhorchak, Jersey City, N. J. [530]; Abraham Waisbrod, New Brighton, L. I.

The same issue of the JOURNAL, namely, that of December 1928, carried announcements of the passing of two distinguished British pharmacopœial workers, Edmund White and Sir Nestor Tirard. *The Pharmaceutical Journal and Pharmacist* said editorially that "there will always stand out to the credit of Edmund White's memory his great and enduring work for education, the decisive stand he took against the practical exclusion of official pharmacy from the work of Pharmacopœial revision, which, endorsed as it was by the Society's Council, undoubtedly precipitated the reorganization of the machinery for this purpose, of which pharmacy now forms an integral part." The name of Sir Nestor Tirard is familiar to American pharmacists chiefly through his joint editorship (with Prof. H. G. Greenish) of the British Pharmacopœia of 1914.

We were shocked by the news of the death of former President John Granville Godding on April 7th. For more than fifty years he was a member of the AMERICAN PHARMACEUTICAL ASSOCIATION and served as its president 1911–1912. A sketch of our late member is printed in the JOURNAL for April, page 433. Another has said of him, "In his service to pharmaceutical organizations, he thinks only of the cause and asks nothing for himself." Mrs. Godding has attended most of the meetings of the ASSOCIATION with her beloved husband. This year she will be absent and will be missed by her many friends. The loss she has sustained will be keenly felt by her this week. As most of you know, Mrs. Godding is a member of our ASSOCIATION.

At our meeting in Portland the veteran member, in years, W. L. DuBois, celebrated his ninetieth birthday. As usual, he was accompanied by his daughter, Miss Charlotte. The meeting was a most happy one for him, for he enjoyed being with his friends. He also contributed a paper at the last meeting published in the January JOURNAL, page 52. The deceased was honorary president of the ASSOCIATION in 1923–1924. Reference to other issues of the JOURNAL speak of the esteem in which Mr. DuBois was held.

Thomas Nevin Jamieson contributed largely to fraternal relationships by founding the Chicago Veteran Druggists' Association. Under the direction and from the pen of Wilhelm Bodemann we have a number of contributions in his memory. An article by the latter on his favorite topic appears in the August JOURNAL.

William Henry Rogers, one of the signers of the Incorporation Certificate of the A. PH. A., a former honorary president of the ASSOCIATION, died January 24th. Those who knew him best speak of him as a man of sterling qualities. A sketch is printed in the August JOURNAL for 1926, and also in that of January 1929.

Dr. Albert Schneider died October 27th, from cerebral hemorrhage. Few members of our ASSOCIATION, or, for that matter, men in other professional lines, have contributed more to the literature of their respective activities than he did. Always active and energetic and seeking information, his years were fully occupied. A sketch of the deceased is printed in the November JOURNAL, 1928. Extended comments could be made relative to all of the deceased, but the references made to the issues of the JOURNAL in which sketches of them appear will serve the purpose better.

The attention of publishers and authors has been called to a coöperative service by inscribing copies of their publications for the AMERICAN PHARMACEUTICAL ASSOCIATION and in this way widening their circle of acquaintance and develop the library service. Doubtless individuals, rather than realize that their libraries will be of little value after their passing, prefer to donate part of their collections to the Headquarters; others have duplicates or historic volumes which they would like to leave to posterity.

Very few of the State and National Associations have made provisions for taking care of books, apparatus and historical material and will be glad to have a repository for them in the Headquarters. This will speak for the collection of such items in all of the states and contribute to the upbuilding of the Headquarters library and museum, and serves as a suggestion to these

organizations—that they have a part in these projects, that their contributions represent an active participation in the institution which they have made possible—reflecting credit to themselves and American pharmacy.

Dr. F. B. Kilmer has contributed a paper to the program of this Section on "The Birth of the Scientific Journal." The paper is based upon an early scientific journal, which was published in France in the 17th Century under the title of *Journal des Scavans*. Dr. Kilmer will present a bound volume of the issues of this Journal for the year 1678 to the ASSOCIATION.

Chairman Scoville has given to the ASSOCIATION a full set of proof sheets, etc., of the A. PH. A. Recipe Book,[1] and has set aside for later delivery, the Circular Letters and other matter connected with the revision of the National Formulary.

Quite a number of historical papers have been printed in the JOURNAL since the last meeting and have added to the interest and value of the publication.

We are meeting here in a rather new section of the country where we can compare the present with the past, not only as far as developments in the industries and agriculture are concerned, but also in professional life. We can here view the up-to-date pharmacy and hear of, if not see, the primitive drug stores in which some of our members were engaged. They labored with a purpose to advance pharmacy and we know how well they have succeeded; they endured the hardships of an undeveloped country and brought about conditions which compare very favorably with those of other states. A number of pharmacists of South Dakota have had a part in our ASSOCIATION work and we have as our presiding officer one of the foremost retail pharmacists of South Dakota and the United States.

The Historian called attention to a gift made to the Section by President D. F. Jones of an old scale used on a whaler many years ago, and also a siphon for drawing off cod liver oil. He also received from Dean G. L. Curry a book formerly of the library of Emil Scheffer, by Frederich Mohr on "Chemical-Analytical Titration Methods." He desired to thank the donors.

Prof. E. Perrot has sent pictures of the museum in the Paris School of Pharmacy. These pictures are interesting because the Headquarters will have a museum. The Historian also exhibited a photograph on an old show globe from the Apothecaries' Hall at New Haven. He also referred again to the Mercer Apothecary shop which has been restored; many items of the Revolutionary period have been donated to the ASSOCIATION having in charge the restoration of historical buildings in Fredericksburg. The Historian also exhibited a photograph of the John Wesley Chapel in Bristol, England, and called attention to the fact that John Wesley had compiled a Formulary which went through a number of editions. He also exhibited a photograph of Dr. Dragendorff who was largely responsible for the Hanbury Medal.

William B. Day remarked that he did not know John Wesley had written a Formulary but referred to the statement of Oliver Wendell Holmes that "John Wesley believed in sulphur and salvation."

Chairman Kebler appointed a Committee on Nominations as follows: William B. Day, L. L. Walton and W. O. Richtmann.

The reading of papers followed:

"Physics in Pharmacy. Part II," by John Uri Lloyd, Wolfgang Ostwald and Walter Haller. (It is printed in the September JOURNAL on pages 862 to 875.)

"Writing Pharmaceutical Biography and History," by Edward Kremers. (It is printed on pages 1032–1037 of the October JOURNAL.) Appreciation of the paper was expressed by Secretary Beal, Chairman Kebler, E. G. Eberle, E. L. Newcomb and others.

Dr. Kremers also contributed a paper on "Tom, the Doctor's Apprentice." He also presented a paper on "LaMort's Pharmacia" which, as far as he was able to learn, is the first textbook on pharmacy that is so designated. He also donated four cuts from this book. The thanks of the Section were extended to Dr. Kremers. He presented another paper "Flueckigeriana, IV: Lloyd's Conference with Flueckiger in New York."

A paper on "The Birth of the Scientific Journal," by Fred B. Kilmer was read by title. The Historian remarked that Dr. Kilmer intended to present a volume of the Journal to the ASSOCIATION. Dr. Kremers said that there were older Journals in the library of the University of Wisconsin. He contended that chemists prided themselves in being modern scientists. In his

[1] Since then, through the courtesy of Editor Ivor Griffiths, copy and proof sheets, which were on display at Rapid City, have been presented to the ASSOCIATION.

opinion, the frequent statement, that chemistry became a science in 1887, is unfortunate. When we say that experimental science was introduced in the 17th century we forget Archimedes' experimentation. He said that one of the best things teachers can do is to have their students repeat this experiment as nearly as it can be duplicated. He said we are prone to think that all science worth while is of comparatively recent date.

"History of Sharp & Dohme, 1845–1929," by Alfred R. L. Dohme, and "Reminiscences of Early Pharmacy in Baltimore," by David M. R. Culbreth, were read by title.

The First Session of the Section on Historical Pharmacy was then adjourned.

SECOND SESSION.

The Second Session of the Section on Historical Pharmacy was convened by Chairman Lyman F. Kebler at 9:00 A.M., August 29th.

The first number of the program was an illustrated lecture on "Kava-Kava (Piper methysticum) Its Ceremonial Uses in the Samoan Islands" (illustrated by lantern slides) by J. T. Lloyd. A vote of thanks was given to Dr. Lloyd.

"History of the Illinois Pharmaceutical Association," by William B. Day.

Charles H. Avery stated that he had been identified with Illinois Pharmaceutical Association for many years and he appreciated the pains which Secretary Day had taken in writing this comprehensive history.

Frederick J. Wulling said that other states should follow Secretary Day's example in writing history of their respective associations.

Chairman Kebler called attention to the value of such contributions for those who search for information relative to legislation. He is now engaged in compiling food and drug legislation.

The next paper was by H. C. Christensen on "Reciprocity in Pharmaceutical Licensure." It was read by title.

"Pharmacy in West Virginia," was the subject of a paper by Roy B. Cook. The author stated that it was too lengthy for reading at this meeting and he presented it as a record.

The next paper was by Robert J. Ruth on "Pharmaceutical History Is Being Made." (Discussion.)

The next paper of the program was "Garth's Dispensary," presented by Frederick J. Wulling for his son, who is the author of the paper. The Dean presented an abstract of the contribution.

The report of the Committee on Nominations presented the following as nominees:

Chairman, George D. Beal, *Secretary*, John Thomas Lloyd, *Delegate to the House of Delegates*, Lyman F. Kebler. The nominees were elected in regular order.

The reading of papers was continued:

"Medical and Pharmaceutical Knowledge by Balzac," by L. E. Warren. (Abstract.)

Secretary Beal gave brief abstracts of the following papers:

"Garcia da Orta and the First Description of Asiatic Plant Drugs," by a European, by Louis H. Roddis.

The following papers were presented by title by Lyman F. Kebler: "Drug Legislation" and "George Thorndike Angell, the Fearless Pioneer for Pure Food and Drugs, and the Friend of Those Who Could Not Speak for Themselves."

The Final Session of the Section on Historical Pharmacy was then adjourned.

Appointment of Japanese Pharmacist General.—The highest rank of pharmacist in the Japanese Army and Navy has been equal to that of the major general. In the Army, however, further improvement has been recently made. (See article in October JOURNAL A. PH. A., page 1046.) After due revisions have been made in the regulations concerning the status of pharmacists in the Army, Dr. Matajiro Watanabe, head of the Army Health Material Arsenal, has become the first Pharmacist General (whose rank is equal to that of lieutenant general under date of September 17th.—*Japanese Weekly Druggist.*

Dr. David I. Macht has been elected to full regular membership in the Optical Society of America in recognition of his original contributions to the physiological, pharmacological and therapeutic effects of ultraviolet and other forms of light.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1929–1930.

Office of the Secretary, 10 West Chase Street, Baltimore, Md.

LETTER NO. 2.

October 29, 1929.

To the Members of the Council:

(*Motion No. 1*) *It is moved by Eberle that the minutes of the first meeting of the Council, 1929–1930, presented in Council Letter No. 1, be approved.*

21. For the information of new members of the Council it is pointed out that motions made by mail in the interim between meetings of the Council require no second.

22. Investment of Funds. The following cash balances are now held on deposit in the several Permanent Funds of the ASSOCIATION mentioned:

Endowment	$1,000
Centennial	1,000
Life Membership	3,500
Research	18,000
Procter Monument	1,000
Remington Honor Medal	1,000

The treasurer has been offered the following bonds which meet the requirements of Article IV of the Constitution and are rated as AAA and recommends that he be authorized to invest the cash balances listed above in these securities as available:

City of Chattanooga, Tenn., 4½% due July 1, 1937, on about 4.90 basis.

City of Dallas, Tex., 4½% due May 1, 1937/67 on about 4.65–4.75 basis.

State of North Carolina, 4½% due Jan. 1, 1950, on about 4.45 basis.

State of North Carolina, 4¾% due Oct. 1, 1963, on about 4.50 basis.

State of Tennessee, 4½% due Feb. 1, 1939, on about 4.60 basis.

City of Newark, N. J., 4½% due Mar. 1, 1952 and 53, on about 4.30 basis.

State of Illinois, 4% due May 1, 1949, 53, 54 and 55 on about 4.30 basis.

State of Missouri, 4½% due Oct. 1, 1948 and 49 on about 4.30 basis.

This recommendation has the approval of the Chairman of the Committee on Property and Funds.

(*Motion No. 2*) *It is moved by Holton that the Treasurer be authorized to invest the cash balances listed above in the securities mentioned as the latter are available.*

23. Applicants for Membership. The following applications properly endorsed and accompanied by the first year's dues have been received.

No. 1, C. B. Allison, 808 Main St., Dallas, Texas; No. 2, Stephen S. Bernatowicz, 7300 Michigan St., Detroit, Mich.; No. 3, Theodore H. Carlow, 416 Naval Ave., Bremerton, Wash.; No. 4, Adam J. Cetnar, 9208 Michigan Ave., Detroit, Mich.; No. 5, A. J. Chmara, 14,633 Warren St., Dearborn, Mich.; No. 6, Jack Chikata, 1718 Dearborn St., Seattle, Wash.; No. 7, Walter Daniel Dembeck, 227 S. Wolfe St., Baltimore, Md.; No. 8, Melvin Dennis, 400 North 43rd St., Seattle, Wash.; No. 9, Joseph Fernandes, 4731 21st Ave., N. E., Seattle, Wash.; No. 10, Edward J. Ferguson, 103 Thayer St., New York, N. Y.; No. 11, L. Frank Gordon, 1020 E. 67th St., Seattle, Wash.; No. 12, Katherine C. Gray, 5720 15th St., N. E., Seattle, Wash.; No. 13, Herbert Hogg, 602 33rd Ave., Seattle, Wash.; No. 14, H. T. Kearney, 719 W. 80th St., Chicago, Ill.; No. 15, Carl Joseph Klemme, School of Pharmacy, Purdue University, Lafayette, Ind.; No. 16, Orvie W. Knott, 3324 Crocker St., Des Moines, Iowa; No. 17, Kenneth E. Lake, 330 Mitchell St., Petoskey, Mich.; No. 18, H. L. Lewis, Hartford, S. Dak.; No. 19, Paul E. Matz, 4754 16th Ave., N. E., Seattle, Wash.; No. 20, Amelia Mesa de Ponce, Calle C No. 182, Vedado, Havana, Cuba; No. 21, Russell C. Morris, 8800 Michigan Ave., Detroit, Mich.; No. 22, M. E. Nichols, 1435 Main St., Oconto, Wis.; No. 23, Felix Nowacki, 8604 Mich. Ave., Detroit, Mich.; No. 24, Claude H. Parker, U. S. Marine Hospital, Stapleton, S. I., N. Y.; No. 25, Henry E. Petersen, Cedar City, Utah; No. 26, Herbert A. Ranowski, 8927 Michigan Ave., Detroit, Mich.; No. 27, Harold Glenn Reiman, 5012 22nd N. E., Seattle, Wash.; No. 28, Helen F. Schroeder, Wesley Hospital, Wichita, Kans.; No. 29, Herman J. Schroeder, 819 Orcas St.,

Seattle, Wash.; No. 30, Herman Shirley, Enderlin, N. Dak.; No. 31, Sister Mary Adelaide, St. Joseph's Hospital, Lorain, Ohio; No. 32, Jack Steele, 1011 W. Saler St., Seattle, Wash.; No. 33, Chester H. Swanson, Route 3, Everett, Wash.; No. 34, Venan E. Thompson, 8400 Michigan Ave., Detroit, Mich.; No. 35, H. S. Waligorski, 19,202 W. Warren Ave., Detroit, Mich.

(Motion No. 3) Vote on applications for active membership in the American Pharmaceutical Association.

24. Applicant for Membership on Account of Contribution to the Headquarters Building Fund. The following non-member of the A. PH. A. has pledged $25.00 or more to the Headquarters Building Fund and has made a cash payment of $5.00 or more. He is entitled to membership and you are requested to vote on the application which has been properly endorsed.

H-1, Henry Harwick, 330 Belmont Ave., Newark, N. J.

(Motion No. 4) Vote on application of contributor to the Headquarters Building Fund for membership in the American Pharmaceutical Association.

E. F. KELLY, *Secretary.*

COMMITTEE REPORTS

REPORT OF THE COMMITTEE ON INTERNATIONAL PHARMACEUTICAL NOMENCLATURE.

Your Committee on International Pharmaceutical Nomenclature, as a whole, has again been inactive in so far as the carrying out of a systematic study is concerned, but it has kept in touch with the developments in this field of endeavor. The committee's reluctance to devote the time necessary to prosecute any extensive studies along these lines may be attributed to the fact that the way to make such studies effective, internationally, has not yet been found.

Our most advantageous point of contact with other nations on matters of pharmaceutical nomenclature has been, and still is, through the Federation Internationale Pharmaceutique; but that organization has not the power to make rulings or to enforce them. It can only act as a center for the dissemination of ideas and opinions. The only organizations endowed with powers of this kind are the committees of revision of the various national pharmacopœias. It would seem, therefore, that in the event the committee should undertake in the future to make a systematic study of some of the problems in this field, it should be carried out with the view to having the results thereof manifest themselves in some authoritative work where they will be brought to the attention of the revision committees in other countries. That authoritative work should be our Pharmacopœia; and inasmuch as a new revision will be started in 1930, it appears that the opportunity the committee has been looking for is at hand.

As stated above, it is the opinion of your Committee that this ASSOCIATION can exercise its greatest influence on the movement for uniformity in pharmaceutical nomenclature by helping to make our Pharmacopœia exemplary in this respect. To attain this objective, the titles of the various items in the Pharmacopœia must be carefully studied, and where there is found a lack of uniformity or consistency, the condition should be corrected. It is probable that legal restrictions or long-established usage will not permit the making of the changes necessary to accomplish this in all cases, but it is believed that conditions can be considerably improved, particularly in the nomenclature of some of the galenicals.

There are a number of instances among the galenicals where a heterogeneous lot of preparations are grouped under one and the same class name, as for example, under the waters, liquors, spirits and tinctures. To remedy this condition, it would appear to be necessary to first formulate exact definitions for the different types of galenicals in question and then to group the preparations accordingly. This is suggested as one of the first studies which this committee might undertake to make. Excellent suggestions for starting the work will be found in an article by Dr. E. Schlumpf, of Zurich, Switzerland, published in the last number of the *Bulletin de la Federation Internationale Pharmaceutique.*

A. G. DUMEZ, *Chairman.*

REPORT OF THE COMMITTEE ON COÖPERATIVE PUBLICITY.

About ten years ago a plan for coöperative publicity was formulated by the national organizations representing the various branches of Pharmacy. Delegates from eight of the national associations met in New York and organized the Drug Trade Bureau of Public Information. This Bureau has functioned at intervals for nearly ten years in the dissemination of information of public interest about pharmacy to the newspapers and magazines of the United States. Its work has been pronounced one of the outstanding constructive achievements in behalf of pharmacy.

The direction of this publicity work to date has been wholly on a volunteer basis. Such meager funds as have been made available by the annual contributions of the national associations have been required for clerical work, mimeographing, postage and occasionally the services of newspaper men.

For several years in succession the amount of space obtained by the Bureau for pharmaceutical news in the public press if bought at the usual advertising rates would have run close to $100,000. The amount of money available for the work of the Bureau has never exceeded $1800 per annum, but by curtailing effort in one year it was possible to do more extensive work the following year. This dearth of funds and the inability of the Director of the News Service to give constantly of his time account for certain lapses in the work. However, at all times since the organization of the Bureau, a close check has been kept on newspaper comment regarding pharmacy, and whenever any serious injustice was done in such comment, steps were taken by the Bureau to remedy the situation. The Bureau is favorably known to newspaper men and its Bulletins are well received whenever offered.

At the last annual meeting of the Bureau held at Washington, in December 1928, steps were taken to resume active work as sufficient funds had been accumulated to warrant a fair expenditure.

At this meeting, Ambrose Hunsberger was elected *President* of the Bureau and H. C. Christensen, of Chicago, was reëlected *Secretary-Treasurer*. Robert P. Fischelis, who has acted as *Director of the News Service* ever since the inception of the Bureau, was reëlected to that office and the work of issuing weekly bulletins to the press is again under way.

Those who are in a position to assist the Bureau in its work are requested to send in pharmaceutical news and information of interest to the public, as well as constructive suggestions whenever possible.

While other professions and business groups are expending anywhere from $10,000 per year upward for publicity work, we are trying to do something for Pharmacy with ridiculously inadequate funds. It is hoped that a repetition of the splendid showing made by the Bureau in recent years will open a source of adequate funds for the kind of campaign that is needed to place Pharmacy before the public in a proper and favorable light.

The continued support of the AMERICAN PHARMACEUTICAL ASSOCIATION in financing this work is earnestly solicited.

(Signed) ROBERT P. FISCHELIS, *Chairman.*

REPORT OF THE COMMITTEE ON HORTICULTURAL NOMENCLATURE.

Your Committee during the past year has continued its work on the list of scientific names and synonyms of drug-yielding plants which it is expected will be completed and ready to submit to the Committee on Standardized Plant Names of the American Joint Committee of Horticultural Nomenclature for inclusion in the next issue of "Standardized Plant Names," sometime next year.

Your chairman of this Committee has been in touch with Secretary Kelsey of the American Joint Committee who expressed pleasure because of the coöperation of this Committee in preparing this list.

Prof. Kelsey reports that the printing bill is nearly paid off and that his Committee has about a thousand copies of Standardized Plant Names for sale to liquidate the small balance and start a fund for the cost of the future edition.

The Committee on "Standardized Plant Names" reports a steady sale for this work but that this will not provide the funds necessary to bring out a new edition at the end of the 10-year

period, 1933, also that about 15,000 or more names will be added to the list in the present work.

The Committee asks that provision be now made for financing the new edition, so that the burden of carrying the printing bills will not be thrown on the shoulders of the few.

In view of the fact that our ASSOCIATION was one of the founders of the American Joint Committee and has since taken some interest in this organization's activities including help in the preparation of "Standardized Plant Names," we recommend that the Council of the ASSOCIATION take action on the request of the Committee on Standardized Plant Names.

A copy of the financial statement of the American Joint Committee on Horticultural Nomenclature as of July 1, 1929 was submitted to the Council.

HEBER W. YOUNGKEN, *Chairman;* CHAS. W. BALLARD, E. N. GATHERCOAL.

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meetings of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten, with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

CHICAGO.

The 184th meeting of the Chicago Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held October 15th at 8:00 P.M. at the Y. M. C. A., 1800 W. Congress Street, with over two hundred (200) in attendance.

The meeting was called to order by President Lindahl, who introduced the speaker, Mr. R. C. Stadelman of the Antivenin Institute.

Mr. Stadelman spoke on Snakes and Snake Venom, illustrated by motion pictures and followed by a demonstration with live, poisonous snakes. The number of snake bites in the United States treated with serum is in excess of 5000 per year, with numerous cases which are never reported. The copperhead, water mocassin and various species of rattle snakes are the most important venomous snakes of the United States. Hardly a state in the country is free from one or another species of snakes and the effects of snake bites are very painful and often terminate fatally. The Texas rattler is the most deadly of the snakes.

The antivenin serum is the only specific means of treatment for snake bites and should be given immediately. One or two syringes, subcutaneously, for an adult and three to five for a child. As an emergency measure, when no serum is available, incision of the wound and suction is the best treatment. Caustics or potassium permanganate should not be used.

The antivenin serum is obtained by inoculating horses with varying amounts of the snake venom to produce the antibodies. The snake venom is previously collected, dried and then dissolved as needed, as the dried venom keeps indefinitely. Likewise, the antivenin serum will remain active for at least five years at room temperature.

Numerous species of live venomous snakes were exhibited, showing their characteristic markings, their fangs, method of striking and habits. Venom was extracted from one of the snakes to show how the snakes are handled and how the venom is used.

The meeting was exceedingly interesting,

educational, fascinating and profitable to the many pharmacists present, and the meeting was adjourned with a rising vote of thanks.

S. W. MORRISON, *Secretary.*

PHILADELPHIA.

The October meeting of the Philadelphia Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was called to order by President Hoch Tuesday evening the 8th, in the P. A. R. D. Building. Reports of the secretary-treasurer were presented and accepted. Chairmen of the various committees reported a number of activities.

Charles Pickett, secretary of the Philadelphia Association of Retail Druggists announced that there would be a meeting of physicians and pharmacists in the P. A. R. D. Building on the evening of November 1st. This meeting is being sponsored by the P. A. R. D. for the purpose of creating a closer feeling and more satisfactory coöperation between pharmacists and physicians. An invitation was extended to all pharmacists to be present and each was asked to bring a physician. President Hoch suggested that for the November meeting of the Local Branch the members join the P. A. R. D. in order that the meeting of pharmacists and physicians may be most successful. This suggestion was discussed and as no opposition was voiced by the members President Hoch announced that the Local Branch would not hold its regular meeting, but would coöperate with the P. A. R. D. on November 1st. He urged the attendance of all members.

Delegate Ambrose Hunsberger, of the Philadelphia Branch, to the annual convention of the AMERICAN PHARMACEUTICAL ASSOCIATION held in Rapid City, S. Dak., during the week of August 26th presented an excellent report on the various convention activities. Prof. E. Fullerton Cook supplemented that of Mr. Hunsberger and reported the meetings of the National Conference of Pharmaceutical Research and the activities of the American Association of Colleges of Pharmacy. Secretary Frank H. Eby spoke of the meetings of the seventh Plant Science Seminar. He stated that more than 40 members and friends of the Seminar were in attendance and enjoyed one of the most interesting and successful meetings in the history of the organization.

The Pharmacy Week program was presented by Raymond Hendrickson. He outlined the radio, newspaper and other activities planned by the general committee. He urged that all pharmacists secure the large maps showing the sources of drugs and display them with crude drugs. He also suggested that crude drug displays be made several times during the year, thereby creating an interest in pharmacy and the pharmacist. Professor Cook stated that the Pharmacy Week Program set a very high standard for the pharmacist and that it was his duty to live up to it.

Charles Pickett gave an interesting report of the annual convention of the National Association of Retail Druggists.

A feature of the evening was a delightful talk by Dr. Charles H. LaWall. In his characteristic manner he described many interesting experiences enjoyed by Mrs. LaWall and himself, while traveling in England, Ireland and Scotland during the past summer. He stated that many regulations and customs established during the World War are still observed. The hours for opening and closing of stores are rigidly enforced. Examinations for pharmacists are very practical and rather severe. A number of Botanical Gardens were visited and these he described in a very interesting way. He displayed a collection of prescriptions which he had collected during his travels. At the close of the talk a rising vote of thanks was extended to Dr. LaWall.

FRANK H. EBY, *Secretary.*

RESEARCH FELLOWSHIP.

A new fellowship in pharmaceutical research has just been established at the Philadelphia College of Pharmacy and Science, carrying with it a stipend of $1000 and free tuition, and applications are being received now from prospective candidates for the college year 1930–31. If an especially well-qualified person is available it is possible that the holder may begin work at the start of the second term of this year, in February 1930.

Persons holding the degree of bachelor of science in pharmacy, chemistry or related subjects are eligible for consideration. The fellowship offers the opportunity for original research under competent direction, and the opportunity to pursue studies leading to the degrees of master of science, master of pharmacy and doctor of pharmacy. The term of appointment for the fellowship ordinarily will be for one college year, but a holder who shows unusual ability may be reappointed for one or more succeeding years, thus permitting him to obtain the higher degrees while holding the fellowship.

EDITORIAL NOTES

Editor: E. G. EBERLE, 10 West Chase Street, Baltimore, Md.

Members of the Council, A. PH. A.: S. L. HILTON, *Chairman;* CHARLES H. LAWALL, *Vice-Chairman;* E. F. KELLY, *Secretary;* H. V. ARNY, A. G. DUMEZ, H. A. B. DUNNING, H. C. CHRISTENSEN, C. E. CASPARI, J. H. BEAL, W. BRUCE PHILIPS, T. J. BRADLEY. *Ex-Officio Members:* D. F. JONES, *President;* A. L. I. WINNE, W. B. GOODYEAR, *Vice-Presidents;* C. W. HOLTON, *Treasurer;* E. G. EBERLE, *Editor of the Journal;* A. G. DUMEZ, *Editor of the Year Book;* R. I. SWAIN, *Chairman of the House of Delegates.*

Collaborators: The Members of the Council; E. FULLERTON COOK, *Chairman,* U. S. P. Revision Committee; ———, *Chairman,* N. F. Revision Committee; the Chairmen of the Sections, A. PH. A.; H. A. LANGENHAN, GLENN L. JENKINS, H. C. NEWTON, DENNY BRANN, GEORGE D. BEAL; A. G. DUMEZ, *President,* A. A. C. P.; CHARLES B. JORDAN, *Chairman,* Executive Committee, A. A. C. P.; JOHN A. J. FUNK, *President,* N. A. B. P.; HENRY C. CHRISTENSEN, *Secretary,* N. A. B. P.

NEW AND NONOFFICIAL REMEDIES.

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the Rules on which the Council bases its action will be sent on application.

W. A. PUCKNER, *Secretary.*

BISMARSEN.—Sulpharsphenamine.—Bismuth.—Bismuth Arsphenamine Sulphonate.—The sodium salt of a bismuth derivative of arsphenamine methylene sulphonic acid (the exact structural formula of which has not been established) with inorganic salts. It contains approximately 13 per cent of arsenic and 24 per cent of bismuth.

Actions and Uses.—For the treatment of syphilis. According to Stokes and Chambers (*J. A. M. A.*, 89 (Oct. 29, 1927), 1500) the drug is somewhat slower in its action than intramuscularly administered sulpharsphenamine or intravenously administered neoarsphenamine, but much more rapid than bismuth. More or less severe pains at the site of injection have been reported.

Dosage.—Bismarsen is administered intramuscularly. The initial dose is 0.1 Gm.; for succeeding doses Stokes and Chambers used 0.2 Gm. each of the drug dissolved in ampul with 1 cc. of sterile distilled water at the time of administration, adding to the solution 2 to 3 drops of a 2 per cent solution of butyn. At the time of reporting, however, the authors questioned the desirability of using the local anesthetic. Weekly increasing to biweekly doses were used in treatment courses of twenty doses.

Manufactured by the Abbott Laboratories, North Chicago, Ill. U. S. patent 1,605,691 (Nov. 2, 1926; expires 1943). U. S. trademark applied for.

Bismarsen is a brownish yellow amorphous powder readily soluble in water, yielding a yellow solution which is slightly alkaline to litmus.

Add 2 cc. of diluted hydrochloric acid to 5 cc. of a 1 per cent solution of bismarsen: a white opalescence appears and dissolves almost immediately; a heavy white gelatinous precipitate develops in two minutes. Add 1 cc. of diluted nitric acid to 5 cc. of a 1 per cent solution of bismarsen: the solution gradually turns brown and yields a precipitate. Add 1 cc. of trinitrophenol solution to 5 cc. of a 1 per cent solution of bismarsen: no apparent reaction takes place (*distinction from silver arsphenamine and potassium bismuth tartrate*). Bubble hydrogen sulphide through a 1 per cent solution of bismarsen: the solution darkens immediately but no precipitate is formed. Add 5 cc. of hydrogen peroxide solution to 5 cc. of a 1 per cent solution of bismarsen: the solution is at first turbid, then becomes a deep reddish brown with formation of a precipitate. Add 1 cc. of mercuric potassium iodide solution to 5 cc. of a 1 per cent solution of bismarsen: the solution yields a greenish yellow opalescence, which in turn assumes a dirty green color on standing. Add drop by drop 2 cc. of a 40 per cent sodium hydroxide solution to 5 cc. of a 1 per cent solution of bismarsen: the solution gradually darkens without any formation of precipitate. Add 0.5 cc. of a 2 per cent silver nitrate solution to 5 cc. of a 1 per cent solution of bismarsen: a dark red solution is produced (*distinction from arsphenamine*). Add 1 cc. of a saturated solution of bromine in water to 5 cc. of a 1 per cent solution of bismarsen: the solution yields a greenish brown precipitate (*distinction from sulpharsphenamine, neoarsphenamine and arsphenamine*). Add 0.5 Gm. of zinc dust and 5 cc. of diluted hydrochloric acid to 0.1 Gm. of bismarsen in a test-tube, at the mouth of the tube hold a strip of filter paper moistened with 5 per cent cadmium chloride solution: the paper turns yellow in four minutes.

Transfer about 0.4 Gm. of bismarsen, accurately weighed, to a Kjeldahl flask, add 2 cc. of sulphuric acid and heat carefully; add 2 cc. of nitric acid a drop at a time, continue heating until brown fumes cease to be given off, cool and add water to make 120 cc., if a white crystalline precipitate appears dissolve it with a few drops of hydrochloric acid; transfer to a 250-cc. beaker, add 7 Gm. of tartaric acid, neutralize with strong ammonia water, add 10 cc. of magnesia mixture followed by 20 cc. stronger ammonia water, allow to stand twelve hours, filter through a hard surface filter paper and wash the precipitate with 50 cc. of 2.5 per cent ammonia water, puncture the filter, transfer the precipitate into a 250-cc. beaker with washings, then add just sufficient hydrochloric acid to dissolve the precipitate, filter, wash the filter well with water, neutralize the filtrate with stronger ammonia water; add 1 cc. of magnesia mixture and 20 cc. of stronger ammonia water; allow to stand twelve hours; filter, using a prepared Gooch crucible; wash with 2.5 per cent ammonia water; dry at 100° C.; ignite at 700° C. for three hours; cool in a desiccator and weigh

as magnesium pyroarsenate and calculate to arsenic: the arsenic content is not less than 12.50 per cent, nor more than 13.50 per cent. Transfer about 0.25 Gm. of bismarsen accurately weighed to an Erlenmeyer flask. Add 5 cc. of diluted sulphuric acid followed by 1 Gm. of powdered potassium permanganate, and 10 cc. of sulphuric acid in small portions; add just sufficient hydrogen peroxide to dissolve the brown precipitate; add 50 cc. of water; boil for twenty minutes; cool to 70° C.; saturate with hydrogen sulphide for twelve hours; filter, using a prepared Gooch crucible; wash the precipitate with water, warm ammonium polysulphide, methyl alcohol, carbon bisulphide and acetone in the order named; dry at 100° C.; cool in a desiccator and weigh as bismuth sulphide (Bi_2S_3); calculate to bismuth: the percentage of bismuth found corresponds with the percentage of arsenic found multiplied by 1.86 (factor As to Bi in $C_{32}H_{32}O_{12}As_2Na_2S_2N_2Bi_2$) plus or minus 0.5 per cent.

From *Jour. A. M. A.* for June 8, 1929.

BIRTHPLACE OF JUSTUS VON LIEBIG TO BECOME MUSEUM.

Last July the Vereinigung Liebighaus was established for the purpose of preserving and maintaining as a museum the rebuilt birthplace of Justus von Liebig in Darmstadt. Memorabilia of Liebig and of others have been brought together in this house. In it also is to be portrayed the development of all those industries which von Liebig established or upon which he had a decided influence. The following are directors of the organization named: A. von Weinberg, of Frankfurt a/M, *Chairman;* E. Berl, of Darmstadt, *Vice-Chairman;* Karl Merck of Darmstadt, *Treasurer;* Councilor in the Ministry K. Lohlein, of Darmstadt, and Mayor Buxbaum, of Darmstadt. Additional auxiliary directors have also been named.

WHAT DRUGS DO YOU USE?

The Committee on Revision of the Pharmacopœia of the United States has mailed a questionnaire to physicians and pharmacists throughout the country requesting them to indicate thereon to what extent there is a professional demand for medicinal products which were official in the eighth or ninth revisions of the Pharmacopœia, but which were not admitted to the tenth revision. The Committee requests pharmacists and physicians to mark O, indicating often, R, implying rarely or N, meaning never, the number of times these medicinal products have been ordered in their stores. Pharmacists and physicians should coöperate with the Committee by answering this questionnaire, and mailing it to Chairman E. Fullerton Cook, 636 South Franklin Square, Philadelphia.

DIGITALIS ASSAY.

The assay of digitalis by various methods with special consideration of Mansfeld's frog-heart sinus method, by A. Stasiak and B. Zboray, *Arch. Exp. Path. Pharm.*, 144 (1929), 283. Comparative assays were made of four digitalis powders using the frog-heart sinus method of Mansfeld and Horn, the six-hour frog method and the cat method. The first method was studied comprehensively and it was found that it is advisable to make comparisons of the resulting values with the international digitalis standard rather than with *g*-strophanthin as suggested by the originators. It is recommended that with each measurement by the sinus method a simultaneous assay be made of a digitalis standard preparation. Conducted in this way the sinus method gave good, consistent results. The differences between the values obtained by the sinus method and six-hour frog and cat methods were of the same general order as those found between the latter two methods. Valuable tabulations list the results.—J. P.—*The Squibb Abstract Bulletin,* Oct. 16, 1929.

THE AMERICAN PHARMACEUTICAL MANUFACTURERS' ASSOCIATION.

Matters of considerable importance in connection with the future publicity and research program of the American Pharmaceutical Manufacturers' Association will be discussed and decided upon at the semi-annual meeting of that organization which will be held in the Hotel Washington, Washington, D. C., December 16 and 17, 1929. The meeting to be held on the first day will be given over largely to problems of executive nature and a general discussion of means and ways of obtaining greater efficiency and economy in distribution.

The second day will be devoted primarily to meeting members of the various Government bureaus and departments with which the members of the Association come in contact in the course of their daily activities. A visit to the Food, Drug and Insecticide Administration, Department of Agriculture and to the Prohibition and Narcotic Divisions of the Treasury Department will occupy the forenoon of December 17th. At the luncheon on this day, Senator George H. Moses will be the guest of honor and will address the members. The afternoon will be devoted to addresses by other Government officials and reading and discussion of the reports of the Research Board and the Contact Committee of the Association.

Among the important topics to be discussed in the executive sessions are: Publicity, the Proposed Census of Dispensing Physicians,

Institutional Advertising and the "Consult your Family Physician" campaign. The officers of the Association are:

President, H. Sheridan Baketel; *Vice-Presidents*, Henry Osterman, E. P. Crowe; *Secretary*, John G. Searle; *Treasurer*, Frank A. Mallett.

OBITUARY.

EDWARD EMERY SLOSSON.

Dr. Edward Emery Slosson, widely known scientist, director of Science Service, and author of "Creative Chemistry," died at his home in Washington, D. C., October 15th, after an illness of several months, aged sixty-four years.

Born in Albany, Kansas, June 7, 1865, he received his degree of B.Sc. from the University of Kansas in 1890 and a Master's degree two years later. Ten years later he received his Ph.D. degree from the University of Chicago. From 1891 to 1903 he occupied the chair of chemistry at the University of Wyoming, and during the same period was also chemist for the Wyoming Agricultural Experiment Station. For seventeen years following, he was literary editor of *The Independent*.

Dr. Slosson was well known for his book, "Creative Chemistry." Among his other writings were "Easy Lessons in Einstein," "Chats on Science," "Sermons of a Chemist," "Great American Universities," "Six Major Prophets" and "Plots and Personalities." He was for eight years a member of the faculty of the Columbia School of Journalism. He was a member of the Authors' Club, of New York and the Cosmos Club, of Washington. Surviving him are his wife and a son, Preston William Slosson, associate professor of History at the University of Michigan.

BOOK NOTICES AND REVIEWS.

Allen's Commercial Organic Analysis—Vol. VII. Fifth edition rewritten, revised and reset. Publishers, P. Blakiston Sons & Co. Editor, C. AINSWORTH MITCHELL. Price $7.50.

This is the seventh volume of the well-known treatise on the properties, modes of analysis, approximate and analytical examination, methods for detection and estimation of impurities, adulterations, products of decomposition, etc. This work is so well and favorably known that a review, except in outline, is unnecessary.

Volume VII has been enlarged over previous editions by 306 pages. The sections on the vegetable alkaloids have been brought together in one volume which facilitates the use of the work in the laboratory. The alphabetical grouping has been adopted in the chemical classification, and the alkaloids have been arranged in the alphabetical order of the names of the plants which produce them and, as far as this is possible, the alphabetical arrangement has been followed throughout. The introduction to the vegetable alkaloids has been prepared by Dr. T. A. Henry, of London, and the general section on alkaloids by T. M. Sharpe.

The several divisions of the alkaloids have been prepared under the editorship of the following: Francis H. Carr, *The Aconite Alkaloids;* E. Horton, *Berberine and Its Associates;* J. J. Fox and P. J. Sageman, *Caffeine, Tea and Coffee;* Oliver Chick, *Cinchona Alkaloids;* Samuel P. Sadtler, *Cocaine;* R. Whymper, *Cocoa and Chocolate;* R. W. Tonkin, *Nicotine and Tobacco;* Frank O. Taylor, *Opium Alkaloids;* C. Ainsworth Mitchell, *Strychnos Alkaloids;* Francis H. Carr, *The Tropine Alkaloids; Atropine and Its Allies, Tropeines* and *Scopoleines.*

As usual each division is complete and comprehensive. The tables of contents of the volumes that have been published can be obtained by writing to the publishers.

Pharmaceutical Formulas. Tenth edition. By S. W. WOOLLEY AND G. P. FORRESTER, published by the Chemist and Druggist, 42 Cannot St., London, E. C. 4. Price 15s., postage 9d.

The fact that "Pharmaceutical Formulas" has gone through 10 revisions is indicative of the value of the book. This edition, as the former revisions, is a collection of new and old formulas for which there is more-or-less demand not only in Great Britain but in all parts of the world. It is a matter of impossibility for a pharmacist to get along without formulas and this publication of more than 1100 pages will be found valuable and useful, because of the careful selection from pharmacopœias and formularies of every country. The greater number, of course, are of British origin. That preparations in demand in the U. S. are listed is indicated by the statement that permission has

been given for using certain parts of the U. S. Pharmacopœia. The publishers do not claim that formulas for preparations which are given under titles similar to those of proprietary remedies are original, and the compounders are cautioned with regard to the use of titles in which a proprietary right is vested.

An alphabetical arrangement is maintained as far as possible, in some instances with reference to the character of the preparations and others are listed according to therapeutic use of the preparation.

Many pharmacists are acquainted with the publication and all of them will find the book of value. The Index is indicative of the number of preparations for which formulas are given; it fills thirty two-column pages.

As stated at the beginning, the very fact that the book has gone through ten revisions speaks for the value of it and being published by the *Chemist & Druggist* gives an added endorsement.

El Indispensable al Farmaceutico. Third edition. By DR. BLAS Y MANADA, Editor of *El Monitor de la Farmacia y de la Terapeutica*, Madrid, Spain. Published by Estanislao Maestre. Price 15 pasetas.

Primarily this book is for Spanish pharmacists, but there is considerable matter contained which gives general information. The book is divided into fourteen parts; the first one is a pharmaceutical calendar. This is followed by a list of maximum doses, also a table of doses according to age and a number of pages are devoted to formulas for infant medication. There is also a veterinary dose table. More than thirty pages are given to Incompatibilities; there is a chapter on Antidotes. The tables on solubilities are quite complete; while in many instances the statements are made that the substance is soluble, very soluble, slightly soluble or insoluble; relative to quite a number of chemicals, however, the extent of solubility is indicated by percentage designation. Twenty pages are given to an alphabetical list of new remedies and synonyms.

A History of the College of Pharmacy of the City of New York. By CURT P. WIMMER, Professor of Pharmacy. Price $10.00.

The JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION is indebted to the College of Pharmacy of the City of New York for a copy of this history. The College was founded in 1829, hence has reached its 100th anniversary. The book is interesting because of the historical data which parallel that of New York City. The illustrations are good and a personal touch is added by bringing into the book a number of letters written by those who had a large part in the development of the College; also of the drug business of New York in its several divisions. Some of the illustrations are designed to show the development of the school from its beginning and the reader is made acquainted not only with the members of the faculty up to the present time, but also with those who had a part in the development of this institution. A roster of the graduates is given from 1831 to the present time, also of the members of the College. Brief sketches are included of members of the faculty. The History has value for all libraries and, particularly, in that of the AMERICAN PHARMACEUTICAL ASSOCIATION. The thanks of the ASSOCIATION are extended for the donation.

A Text Book of Pharmaceutical Arithmetic. By THEODORE J. BRADLEY, Dean of the Faculty and Professor of Chemistry in the Massachusetts College of Pharmacy. 200 pages. Published by Lea & Febiger, Philadelphia. Price $2.25.

The author states that pharmacists care little or nothing about the theory of arithmetic, so the subject is presented by examples and practice, omitting theoretical discussion almost entirely. The scope of the book was determined by the outlines of pharmaceutical arithmetic in the "Pharmaceutical Syllabus," and in "Basic Material for a Pharmaceutical Curriculum." There are fifteen chapters and a presentation of the subject begins with ratio and proportion and ends with the mathematics of chemical problems. The chapter on ratio and proportion opens with a number of general statements and explanations, and then problems follow. Calculation for one or more are shown and others, which come under the same procedure, are to be solved by the student. In other words, this is the plan followed throughout in the book for teaching this important subject. The section which deals with weights and measures, wherein the different systems are explained, is followed by other chapters which show relationship of the various systems. The thought is carried throughout the book that its purpose is for teaching the pharmacy student, hence, the problems are based on calculations that apply to the prescription department and the laboratory.

Glancing through the book the writer is impressed with its value as an aid to the student in a subject wherein many are deficient.